Cleveland Clinic Quarterly

A Bulletin Published by
The Staff of the Cleveland Clinic
CLEVELAND, OHIO

Vol. 13 JULY, 1946 **No. 3**

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Issued in four n rs during the year; one in January, one in April, one in July and one in October by veland Clinic Foundation, 2020 East 93rd Street, Cleveland 6, Ohio.

] d as second-class matter March 4, 1935, at the Post Office at Cleveland, Ohio, under the Act of August 24, 191.

THE TREATMENT OF LYMPHOID HYPERPLASIA OF NASOPHARYNX BY RADIUM

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Many patients have developed excessive hyperplasia of lymphoid tissue in the pharynx and nasopharynx, predisposing them to frequent colds, deafness, otitis media, chronic nasal congestion, and postnasal discharge. Why this hyperplasia occurs in some persons and not in others is not clearly understood. The condition is usually seen in patients who have had repeated attacks of upper respiratory infections and their complications.

Surgical removal of tonsils and adenoids has been an accepted form of treatment for many years and of unquestionable value in properly selected cases. However, in many of these cases the hyperplasia has continued to develop postoperatively. Repeated attempts at surgical removal of lymphoid tissue have often been hazardous to the patient, as too extensive removal of lymphoid tissue can result in scar tissue formation, and damage to the eustachian tube orifice may result in permanent closure.

The most rational approach to the treatment of lymphoid hyperplasia in the nasopharynx has been advocated by Dr. S. J. Crowe of Johns Hopkins Hospital.

The main problem is to remove the hyperplastic lymphoid tissue, which is often diffusely spread throughout the entire nasopharynx and postnares or localized in the fossa of Rosenmüller or eustachian tube orifice. These regions are inaccessible for surgical removal. As lymphocytes are very radiosensitive, a small dosage of gamma and beta rays is sufficient to inhibit mitosis in the germinal centers and thus stop the formation of new lymphocytes. The dose is small, therefore there is no danger of damage to the nasopharyngeal mucous membrane. Crowe's observations lead him to believe that lymphocytes, like skin cells, have a brief cycle and that under irradiation no new lymphocytes are formed to replace the old. The lymphoid mass shrinks and finally disappears, leaving the area covered by mucous membrane.

As Crowe has pointed out, it is not so much the size but the location of lymphoid nodules that is important. Small nodules in the fossa of Rosenmüller, about the pharyngeal orifice, or the area between the tubal orifice and the posterior end of the middle turbinate, may seriously impair the ventilating function of the eustachian tubes.

The nasopharynx is the most important location of a primary focus of infection in the upper air passage. This is due to the rich content of lymphoid tissue in the mucous membrane and to the proximity of the nasopharynx to the nasal passages, accessory nasal sinuses, and eustachian tubes.

Complications encountered with lymphoid hyperplasia of the nasopharynx are: recurrent colds, chronic rhinitis, chronic tracheobronchitis, sinusitis, asthmatic bronchitis, deafness, chronic or recurrent otitis media, and mastoiditis. In addition there are those due to purely mechanical causes, chiefly aero-otitis or barotrauma, which was encountered so extensively in our air force during the war.

Examination of Nasopharynx

This portion of the upper air passage is not easily examined. In most adults and some children a satisfactory view can be obtained with a mirror. However, in many the nasopharyngoscope is essential for a complete inspection. Occasionally in children with impaired hearing general anesthesia has been used to obtain a satisfactory examination. It is important to shrink the nasal mucous membrane and to remove all excess nasal secretions before applying a local anesthetic, as less topical anesthetic will then be necessary. The insertion of the pharyngoscope through a perforation in a napkin or piece of folded gauze will afford some protection to the examiner.

During the examination the orifices of the eustachian tubes should be clearly seen, as should the vault of the nasopharynx, posterior end of the septum, and the area both anterior and posterior to the tubal orifices.

The fact that the tonsils and adenoids have been removed or that the tonsillar fossae and pharynx appear normal does not mean that lymphoid tissue is absent in the nasopharynx. If a very large adenoid is present it is safer to remove the mass surgically and follow with irradiation, since less radium treatment will then be necessary. In the presence of an acute infection, irradiation should be postponed for approximately four weeks. In cases of marked degrees of chronic infection the first treatment is given in two doses one week apart. If these precautions are observed acute otitis media will rarely develop immediately after the radium treatment.

Lymphoid tissue in the nasopharynx, especially when located near the eustachian tube orifice, interferes with proper functioning of the tubes and predisposes the patient to frequent colds, chronic rhinopharyngitis, chronic closure of the eustachian tubes, otitis media, and deafness. Crowe and his associates in a study of 1365 children between 8 and 13 years of age found that more than 75 per cent had a pronounced

recurrence of lymphoid tissue in the nasopharynx following tonsillectomy and adenoidectomy. This was due to the inability to remove completely the lymphoid tissue by surgical means.

Because of the complications that frequently accompany the presence of this lymphoid tissue, it should be eradicated by the most effective means which will produce no harm to the patient. Both x-ray therapy and irradiation by radium have been used.

It is difficult to deliver enough roentgen rays to the nasopharynx, as approximately one-half of the rays delivered to the neck are absorbed by the soft tissues before they reach the nasopharynx. Several portals must be used in order to prevent skin irritation. This excessive dosage subjects the ossification centers of the skull and face bones to a large amount of radiation. It is also difficult to keep young children in a position for accurate cross-firing for the entire treatment. Good results cannot be expected unless the maximum intensity of treatment is delivered in and around the orifice of the eustachian tube.

In contrast to the x-ray, the radium nasal applicator can be placed on the exact spot where the treatment is most needed (fig. 1). Under local anesthetic the applicator is passed along the floor of the nose until the tip touches the posterior pharyngeal wall. Because of the sensitivity of lymphocytes to beta and gamma irradiation, the dosage employed is so small that there is no danger of a burn or of drying the mucous membrane.

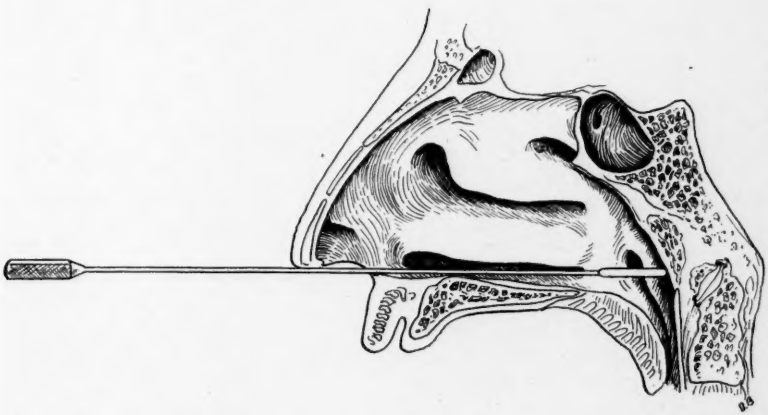

FIG. 1. Schematic illustration of nose and nasopharynx showing position of radium applicator during a treatment.

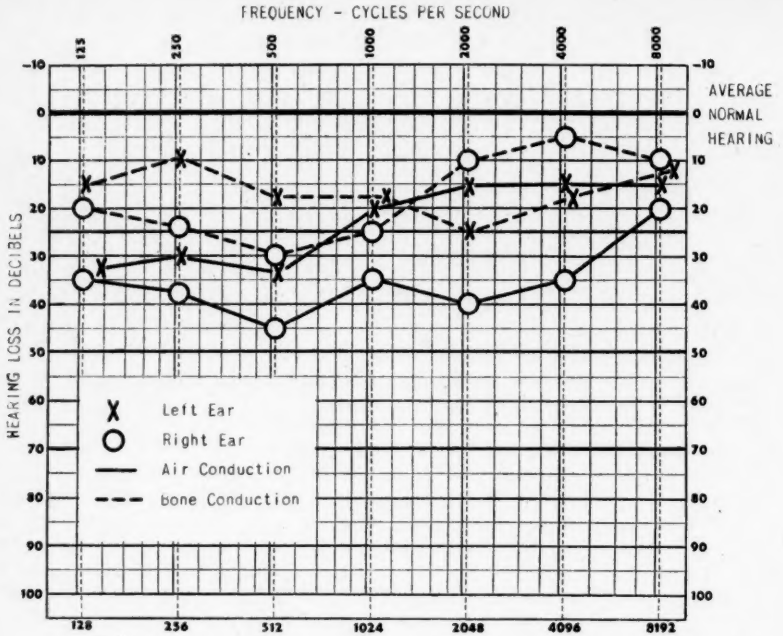

FIG. 2. Case 1. Audiogram before treatment reveals bilateral conductive deafness more marked in right ear.

Case Reports

Case 1. A 9-year-old girl was brought to the Clinic with the chief complaint of deafness of two months' duration. There was no history of otitis media or unusual childhood disease. Physical examination was negative except for lymphoid hyperplasia of the nasopharynx and moderately retracted membrana tympani. Tonsils and adenoids had been removed. Audiogram revealed bilateral conductive deafness (fig. 2).

The patient was given 3 applications of radium to the nasopharynx at monthly intervals. An audiogram six weeks later revealed normal hearing bilaterally (fig. 3).

Case 2. A 12-year-old boy was brought to the Clinic with the complaint of discharging right ear of one week's duration. This had been preceded by a severe upper respiratory infection. Past history revealed numerous similar attacks since early childhood, even though tonsillectomy and adenoidectomy had been performed. Physical examination was negative except for a diffuse lymphoid hyperplasia of the nasopharynx and a reddened, edematous, bulging right tympanic membrane.

The acute phase was treated by chemotherapy, and four weeks later the patient was given his first radium treatment, although the ear was still draining. An audiogram taken at the time of the first treatment revealed bilateral conductive deafness (fig. 4).

Four weeks after the first radium treatment the right ear was no longer draining. After 3 radium applications the eustachian tubes were found to be well open to the insufflation of air, and the audiogram taken one month after the third treatment revealed normal hearing bilaterally (fig. 5).

Case 3. A 9-year-old boy was brought to the Clinic with the complaint of deafness of the right ear of nine months' duration. There was no history of otitis media. Physical examination revealed the tonsils large and the orifices of the eustachian tubes obscured by the adenoids. Tympanic membranes were retracted. Eustachian tubes were not well open to the insufflation of air. Audiograms revealed a mixed type of deafness of the right ear (fig.6).

The enlarged tonsils and adenoids were surgically removed and subsequent radium applications given to preserve as much hearing as possible. An audiogram immediately following the fourth treatment showed improvement of hearing in the right ear (fig. 7).

During the past two years a total of 144 patients have been treated at Cleveland Clinic for lymphoid hyperplasia of the nasopharynx according to the method advocated by Crowe and his associates.

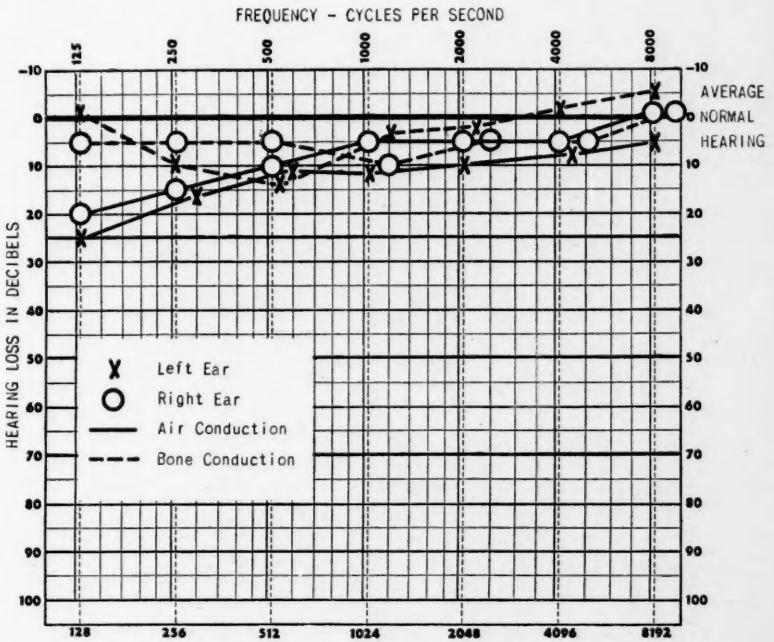

FIG. 3. Case 1. Audiogram reveals essentially normal hearing six weeks following third radium treatment.

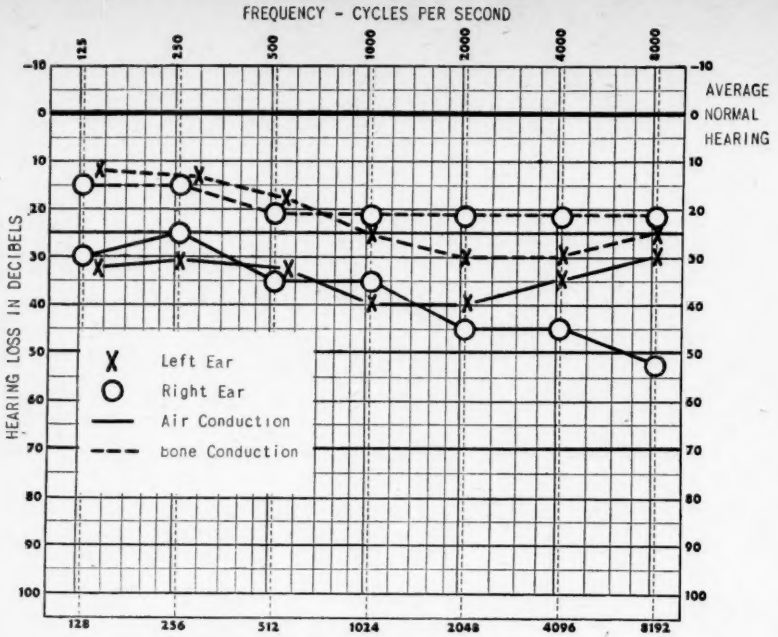

FIG. 4. Case 2. Audiogram reveals bilateral conductive deafness with air conduction at 30 to 40 decibel level in both ears.

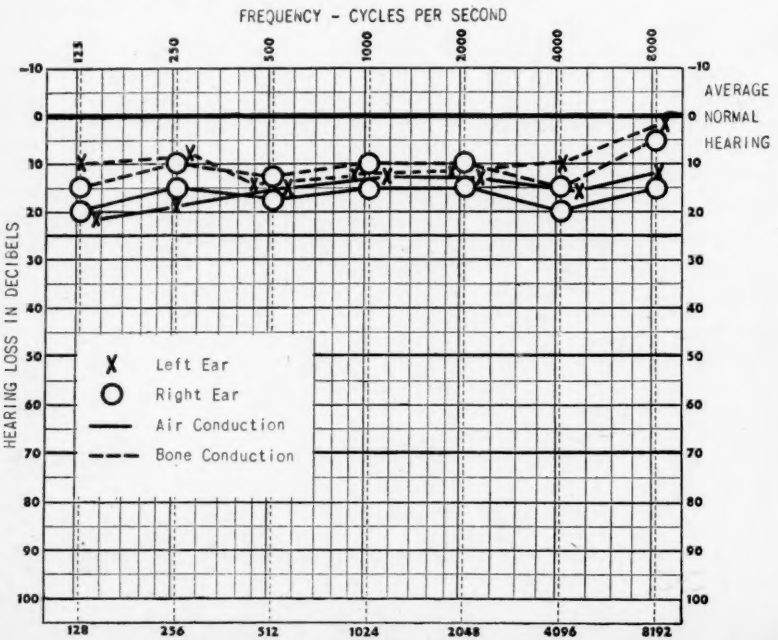

FIG. 5. Case 2. Audiogram one month after third radium treatment reveals hearing has returned to normal range.

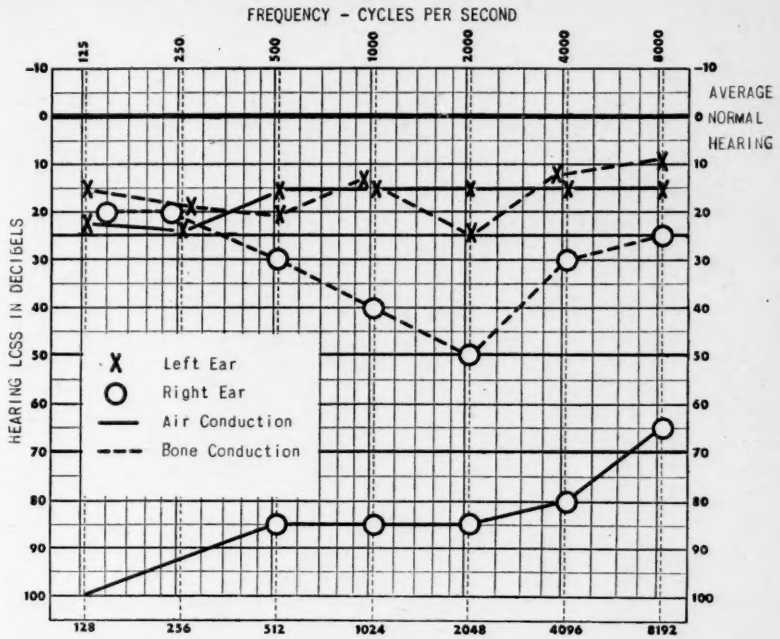

FIG. 6. Case 3. Audiogram reveals pronounced hearing loss of the mixed type in the right ear. Normal hearing in the left ear.

The dosage used was 2 gram minutes to each side of the nasopharynx, repeated for 3 to 4 treatments at monthly intervals. The first 42 cases were treated with an applicator having a brass filter of 1 mm. thickness prepared by Dr. Otto Glasser of the Research Division. This was later replaced by a smaller applicator of monel metal 25 cm. long and having a radium containing chamber 15 mm. in length and 2.3 mm. in diameter. This contained 50 mg. of radium. The latter instrument allows passage of more beta rays than the 1 mm. of brass in the radon applicator, but the results are as good and the dosage is constant, eight and one-half minutes on each side. The tip should be held momentarily under a faucet of running water, then dipped in alcohol, again washed with running water, and dipped in oil before inserting it into the patient's nose.

The operator should wear rubber gloves and avoid wiping the applicator with gauze because of exposure to the hands. When the applicator is not in use it should be kept in a lead cylinder.

Cases should be carefully selected for this type of treatment. Indiscriminate use of radium should be avoided. It is not a panacea for all nasal and ear complaints. Whether it will improve the hearing in a given case depends on the type of obstruction of the eustachian tube and the duration of the impairment. Its greatest value is in re-establishing the patency of an eustachian tube which is closed by lymphoid tissue and in preventing repeated attacks of otitis media.

The results have been gratifying in mildly and moderately deaf children, but less so in adults or extremely deaf children.

Using Crowe's method, uniformly good results have been obtained, particularly in children with deafness associated with partial or complete obstruction of the eustachian tubes. There has been a notable decrease in the number of upper respiratory infections and their complications in the patients treated.

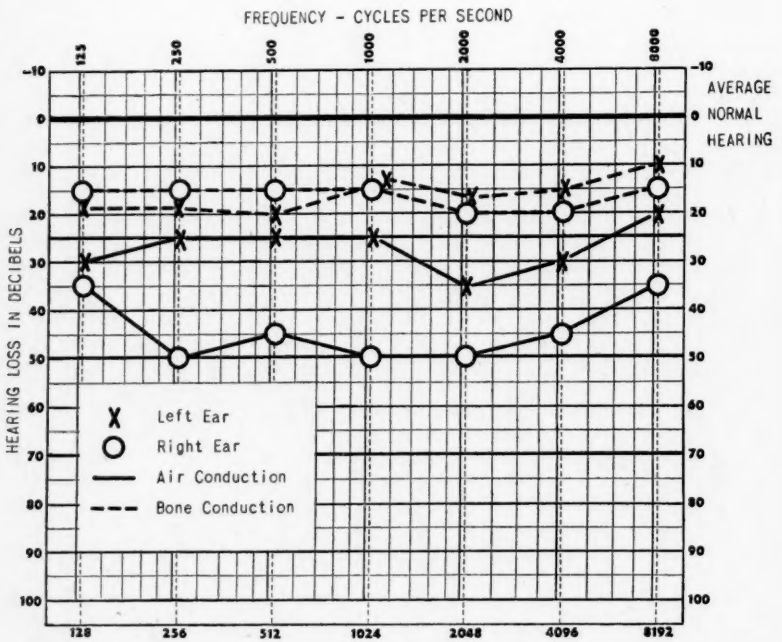

Fig. 7. Case 3. Following the fourth radium treatment the audiogram showed definite improvement in the right ear but not to normal range.

PROGNOSTIC SIGNS IN EXPERIMENTAL HEMORRHAGIC SHOCK

OTTO GLASSER, Ph.D., and IRVINE H. PAGE, M.D.
Research Division

Despite a large amount of investigation, criteria have not been found which indicate with certainty the death or survival of animals in secondary hemorrhagic shock. This has handicapped efforts to ascertain the value of various treatments. It was, therefore, the purpose of this investigation to study still other manifestations of shock in the hope that their quantitative measurement would lead to better prognosis.

Methods. Dogs were anesthetized by subcutaneous injection of 5 mg./kg. of morphine sulphate and intraperitoneal injection of 30 mg./kg. of sodium pentobarbital. The animals were bled rapidly from the femoral artery until, within a few minutes, an arterial pressure of 50 mm. Hg was established. This level was maintained for ninety minutes, after which it was lowered to 30 mm. Hg by further withdrawal of blood. This was maintained for forty-five minutes or more, making the total period of hypotension at least one hundred and thirty-five minutes, the average period being one hundred and forty-seven minutes. The withdrawn blood was stored in a bottle-reservoir under controlled pressure and remained connected with the arterial circulation for the duration of the experiment. The quantities of blood removed to produce the desired state of hypotension ranged from 2.6 to 7.7 per cent body weight. Ten to 15 mg. of heparin was used as anticoagulant in the reservoir and connecting tubing in each experiment.

After the hypotensive period, all or part of the blood was reinfused through the same femoral artery at an average rate of 30 ml. per minute, until the dogs' arterial pressure was re-established at about 100 mm. Hg. The amount of blood necessary to accomplish this ranged from 20 to 100 per cent of the withdrawn blood. Kymographic records of arterial pressure, volume of blood in the reservoir, and respiratory rate were obtained for the entire experiment (fig. 1, 2).

Results. Among various prognostic criteria studied the following proved most useful:

1. Any persistent drop of arterial pressure during the hypotensive period, which causes blood to flow back from the reservoir into the animal, must be considered a bad prognostic sign for survival. In particular, the larger the intake of blood by the animals during the last fifteen minutes of the 30 mm. hypotensive period, the smaller their chance for indefinite survival. This sign is critical and should be obtained from continuous kymographic records of both volume in the reservoir and arterial pressure during this period. The correlation factor between

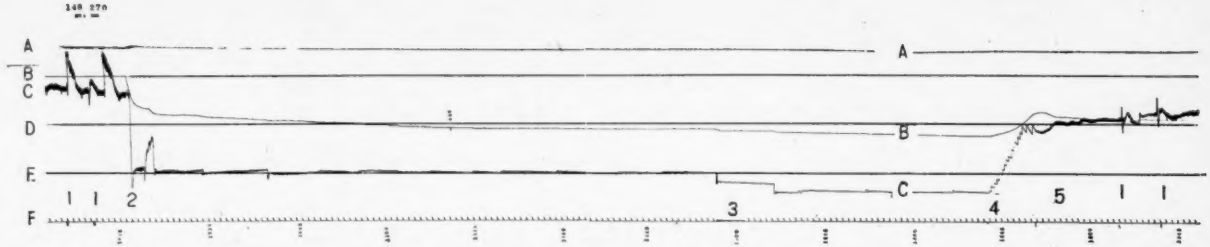

FIG. 1. Kymographic record of experiment 148-270 (April 4, 1946): A. respiration; B. blood volume in reservoir, with base line at 150 mm. Hg; C. arterial pressure; D. 100 mm. Hg line; E. 50 mm. Hg line; F. 0 mm. Hg base line, with time intervals of 1 min. Duration of experiment 3 hrs. and 45 min. Experimental procedures: 1, response of arterial pressure to adrenalin; 2. bleeding to establish arterial pressure of 50 mm. Hg; 3. additional bleeding to establish arterial pressure of 30 mm. Hg. Total time of hypotension: 146 min.; 4. arterial transfusion; 5. ouabain. Prognosis for survival good on account of no intake of blood during hypotensive period, small intake during transfusion, good return of adrenalin response. Result: animal survived and recovered completely.

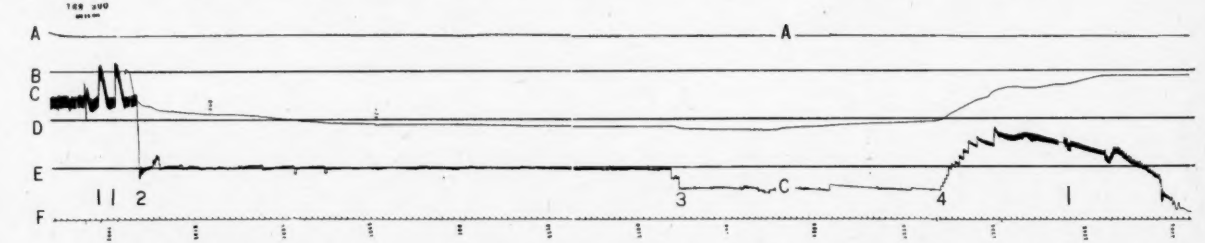

FIG. 2. Kymographic record of experiment 163-300 (April 25, 1946): A. respiration; B. blood volume in reservoir, with base line at 150 mm. Hg; C. arterial pressure; D. 100 mm. Hg line; E. 50 mm. Hg line; F. 0 mm. Hg base line, with time intervals of 1 min. Duration of experiment 3 hrs. and 12 min. Experimental procedures: 1. response of arterial pressure to adrenalin; 2. bleeding to establish arterial pressure of 50 mm. Hg; 3. additional bleeding to establish arterial pressure of 30 mm. Hg. Total time of hypotension: 137 min.; 4. arterial transfusion; 5 ouabain. Prognosis for survival poor on account of considerable intake of blood during latter part of hypotensive period, large intake during transfusion, poor return of response to adrenalin. Result: animal died 30 min. after transfusion.

the intake in milliliters and indefinite survival for our 68 dogs was —0.55 ± 0.07.

2. The larger the response of arterial pressure to a dose of 0.1 to 0.2 ml. of a 1:10,000 adrenalin solution after reinfusion of blood compared with the response to an identical dose given before bleeding, the better the chance for indefinite survival. The correlation factor between return of adrenalin response and permanent survival was +0.54 ± 0.07.

3. The larger the intake of blood by the animals during arterial reinfusion required to establish an arterial pressure of 100 mm. Hg, the smaller their chance for survival. The average intake of animals with bad prognosis was 50 per cent higher than for those with good prognosis.

On the basis of these three criteria, 26 out of the 68 dogs were given a bad prognosis and 42 a good one. All of the former died from terminal shock within less than ten hours after reinfusion. Ouabain, 0.05 mg./kg., was given shortly after infusion to 12 animals of this group but produced no effect upon their time of survival.

Of the 42 dogs with good prognosis, one group of 28 was given ouabain shortly after infusion; 20 dogs, or 71 per cent of this group, survived indefinitely. Of the remaining 14 dogs which did not receive ouabain only 5, or 36 per cent, survived indefinitely.

For all surviving dogs the amount of blood necessary to re-establish an arterial pressure of 100 mm. Hg after their hypotensive period was about 30 per cent less than the original amount of blood withdrawn. Attempts to infuse the remaining amount of blood led frequently to undesirable symptoms ordinarily observed in overtransfusion.

Summary

A group of 68 mongrel dogs was submitted to severe hemorrhagic shock and subsequent intra-arterial infusion of part or all of the removed blood. Three criteria permitted prediction of the probable fate of the shocked animals. These were: (1) persistently falling arterial pressure during the hypotensive period, causing blood to flow back from the reservoir into the animal indicates small chance for survival; (2) the more nearly normal the pressor response to adrenalin after restoration of arterial pressure the better the chance of survival; (3) the larger the intake of blood during arterial reinfusion to establish normal blood pressure, the smaller the chance of survival. All dogs (26) given a bad prognosis on the basis of these criteria died within less than ten hours. Forty-two dogs were given a good prognosis. Twenty-eight of these were given ouabain after infusion and 20 of them, or 71 per cent, survived indefinitely. The other 14 dogs with good prognosis did not receive ouabain and only 5 of them, or 36 per cent, survived indefinitely.

The authors wish to express their appreciation to Anne Worth for her valuable help in these experiments.

THROMBOCYTOPENIC PURPURA IN PREGNANCY; TREATMENT BY SPLENECTOMY AND CESAREAN SECTION

Report of a Case

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Inasmuch as thrombocytopenic purpura is an uncommon disease, its occurrence in pregnancy is even more rare. Since the description of essential purpura by Werlhof in 1775, numerous contributions toward its etiology, diagnosis, and treatment have been made, including the first splenectomy by Schloffer in 1916.

The coexistence of thrombocytopenic purpura and pregnancy has been less widely reported. Polowe in 1944 reviewed the literature and found 62 cases of pregnancy complicated by purpura. However, in 1943 Burnett and Klass found records of 68 cases of which they regarded only 4 as true thrombocytopenic purpura. Finn in 1944 accepted the cases of Burnett and Klass, gleaned 6 more from the literature, and described 3 cases of his own, thus bringing the total to 13 cases. Patterson has recently reported another case. Since an accurate analysis of all reported cases is impossible, and since there are doubtless other unreported cases, it may, nevertheless, be safely assumed that thrombocytopenic purpura in pregnancy is one of medicine's more unusual combinations.

Splenectomy has been performed in a moderate percentage of cases of pregnancy complicated by thrombopenic purpura. As in uncomplicated purpura, the procedure has been followed largely by dramatic improvement. If one is to accept the total number of proved cases of thrombopenic purpura in pregnancy as being in the neighborhood of 15, a study of these cases reveals splenectomy to have been performed in 8.

A careful analysis of the literature has failed to reveal a case of pregnancy complicated by thrombocytopenic purpura in which both splenectomy and cesarean section were performed. For this reason and because of the interesting complications which developed, the following case is presented.

Case Report

A 19-year-old white female, presented herself at Cleveland Clinic, service of Dr. Haden, on December 12, 1945, with the complaints of spots on arms, bleeding gums, and bloody urine. She stated that she had been perfectly well until four weeks previously, when she first noticed bloody urine followed by bleeding from gums and epistaxis. Prior to her admission she had been in another hospital for one week

where blood studies were made, and one blood transfusion and intramuscular injections of blood and glucose were given. During her stay in this hospital purpuric spots developed on the abdomen, thorax, and legs.

She said that she was seven months pregnant, her last menstrual period having occurred May 23, 1945, and had had no previous pregnancies or abortions. Her family history was negative, as was the remainder of the personal history.

Physical examination revealed a well developed and nourished young white female 60 inches tall and weighing 152 pounds, temperature 98°, pulse 84, blood pressure 110/80. The physical examination was essentially negative except for small purpuric lesions scattered over the legs, arms, thorax, and abdomen. Crusted blood was present on the gums and nares; the uterus was palpable 3 cm. above the umbilicus. Fetal heart tones were not definitely heard. The tourniquet test was moderately positive after three minutes, and markedly so after five minutes.

Laboratory studies were as follows:

Blood report:

Red blood cells:
1. Number per cu. mm. 3,250,000
2. Size ..... moderate anicytosis
3. Shape ..... slight anicytosis
4. Color ..... slight pallor
5. Nuclear particles ..... occasional Howell-Jolly body
6. Reticulocytes 4.5%

Volume of packed red blood cells ..... 64% of normal
Volume index 0.98
Hemoglobin ..... 58% of normal (9 Gm. per 100 cc.)
Color index 0.89

White blood cells:
1. Number 8900
2. Differential:
   - Neutrophiles 70%
   - Lymphocytes 10%
   - Eosinophiles 1%
   - Monocytes 8%
   - Basophiles 1%
   - Nonfilamented neutrophiles 7%
3. Abnormal forms:
   - Atypical mononuclears 1%
   - Metamyelocytes 2%

Icterus index 4
Platelets 38,000
Coagulation time ..... 10 minutes (Lee and White method)
Bleeding time ..... more than 10 minutes (Ivy method —test stopped at the end of 10 minutes as there was no evidence of cessation of bleeding)
Prothrombin time ..... 15 seconds
Clot retraction ..... character of clot: moderately firm
Amt. serum expressed in 4 hours: 20%
Extra corpuscular volume: 51%

Urinalysis:

Sp. gravity	1.006
pH	6.0
Albumin	(++)
Sugar	0
Erythrocytes	numerous
Leukocytes	5-10
Blood sugar	85 mg. (¼ hr. p.c.)
Wassermann and Kahn	negative

The patient was admitted to Cleveland Clinic Hospital and given daily injections of parathormone, 2 cc. (200 units) daily. During the first week of admission blood continued to ooze from the nose and gums. A generalized placental bruit could be determined, but definite fetal heart tones were never heard. However, the patient stated that she occasionally felt fetal movements. By the end of ten days her blood platelet count had dropped to 14,000 per cu. mm., by which time she had received 10 injections of 200 units of parathormone and two 500 cc. transfusions of whole blood.

Splenectomy was decided upon, and this operation was performed (R.S.D.) on January 8, 1946, under subcostal block and light ether anesthesia. Except for rather profuse generalized hemorrhage, no particular difficulty was experienced, and the patient tolerated the procedure well.

Following operation blood continued to ooze slightly from the gums and nose, and, in addition, there was evidence of spotty bleeding from the vagina. At this time the patient began to complain of irregular, cramp-like abdominal pains, and no longer felt fetal motion. About the fourth postoperative day she developed tenderness in the right calf and demonstrated a positive Homan's sign. Several days later she complained of sudden pain in the left lower chest, aggravated on inspiration, and a faint transitory friction rub could be heard in this area. A portable x-ray of the chest showed no abnormal changes.

By the eighth postoperative day the vaginal bleeding had increased to rather sizeable clots, and the irregular, cramp-like abdominal pains increased in severity. No fetal heart sounds nor uterine souffle could be heard. The fetal head was free and well above the pelvic outlet, the cervix tough and undilated. Dr. F. S. Mowry of University Hospitals was called in consultation and, in view of the continued vaginal bleeding, undilated cervix, and absence of heart sounds, he believed a partial placental separation had occurred. Normal labor, in his opinion, was apt to be prolonged and disastrous, and cesarean section was advised.

A cesarean section was performed (F.S.M.) under general anesthesia on January 16. The procedure was complicated by tremendous oozing from all tissues. The classical type of operation was employed, and a macerated fetus and a partially separated placenta delivered. The patient again tolerated the operative procedure well.

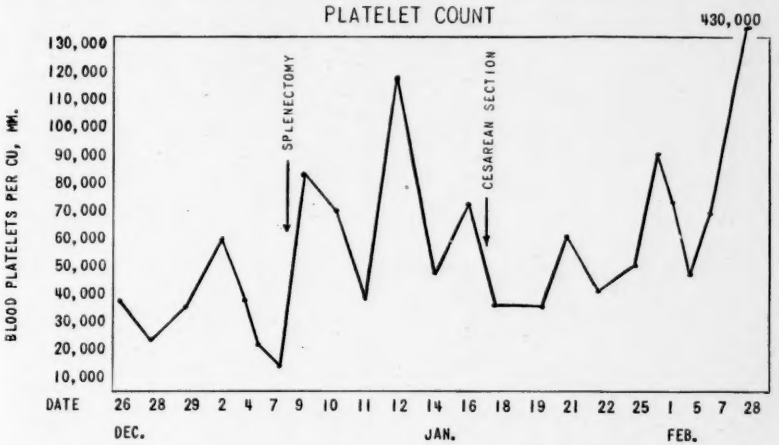
Following operation the patient continued to complain of pain in the left chest. The temperature showed a daily sharp rise despite continued administration of penicillin in doses of 25,000-50,000 units given every two to three hours. An x-ray of the chest on the tenth day after cesarean section showed a pneumonic infiltration along the left border of the heart and a small amount of pleural fluid along the periphery of the left lung.

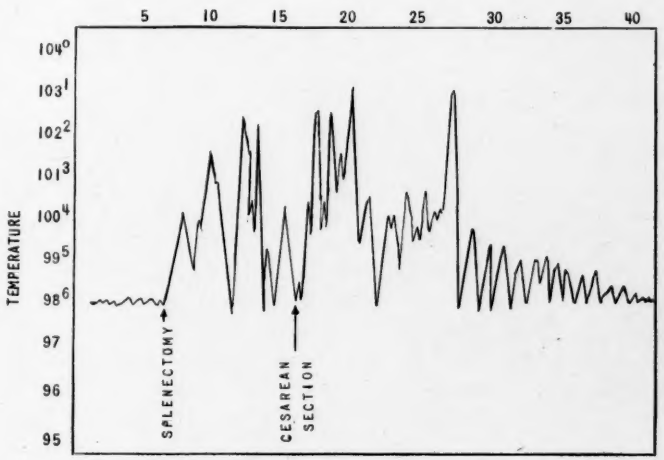
However, she began to improve subjectively, the temperature gradually dropped to normal, and she was discharged from the hospital on the thirty-ninth day after admission.

The blood platelet count and temperature reaction are shown on the accompanying charts. Pathologic report of the spleen was described by Dr. Harry Goldblatt: "Architecture is somewhat altered. The most striking change in the sections is the vascular

disease, which is pronounced. Both large and small arteries have greatly thickened walls due to proliferation of the intima, with partial or even complete hyalinization of the wall. The other striking feature is the variety of cells present both within and between the sinusoids. Here and there are multinucleated cells of the megakaryocytic type and occasional long mononuclear cells which could be Werlhof cells. Diagnosis: Hyperplasia, severe, of spleen (variety of cells)."

The patient returned to the Clinic on March 28, six weeks after her discharge from the hospital. She stated that she was in excellent health and had had no bleeding tendency. Her first postpartum menstrual flow had occurred on March 8, was not pro-





fuse, and lasted four to five days. No ankle edema was present and she experienced only occasional aching of the right leg.

Blood studies at this time were as follows:

Red blood cells	4,680,000
Volume of packed red cells	91% of normal (41 cc. per 100 cc.)
Volume index	0.97
Hemoglobin	75% or normal (11.5 Gm. per 100 cc.)
White blood cells	9550
Neutrophiles	59%
Lymphocytes	39%
Eosinophiles	2%
Monocytes	9%
Basophiles	1%
Presence of abnormal forms	none
Icterus index	4
Platelets	430,000
Coagulation time	12 minutes
Bleeding time	3½ minutes
Clot retraction	firm. 71% serum expressed in 5 hr.

Discussion

Because of its rarity, little is known about thrombocytopenic purpura in relation to pregnancy. Burnett and Klass believe that no causal relationship exists between the two, but rather that thrombocytopenic purpura has periods of exacerbation and remission which may coincide with pregnancy. They believe that it is equally common in multiparas and primiparas, an opinion which is disputed by other writers. They also state that only 1 out of 5 patients had hemorrhagic tendencies prior to the pregnancy, and that these patients had had normal previous pregnancies. Most authors agree that no hemorrhage occurs at the time of delivery, although Mosher maintains that all cases of purpura in pregnancy end fatally because of hemorrhage.

What effect does the thrombocytopenic purpura of the mother have on the child? A wide diversity of opinion exists on this point. Mosher states that 50 per cent of infants die in utero or shortly after delivery. Burnett and Klass believe that purpura occurring in the fetus is not the essential type, but rather symptomatic purpura or the result of a familial platelet defect. Of 13 cases reviewed by Finn, 4 infants died, whereas, in the 9 living infants, only 1 showed evidence of congenital thrombocytopenic purpura. Although it is difficult to determine the prognosis for the infant, it would appear to be better if the disease is in a chronic phase, and if splenectomy has been done prior to pregnancy.

A review of the records of Cleveland Clinic has failed to reveal other instances of pregnancy complicated by thrombocytopenic purpura.

During the past decade this disease has been diagnosed in 40 cases; splenectomy has been performed in 17 of these cases.

Summary

A case of thrombocytopenic purpura complicating pregnancy, treated by splenectomy and cesarean section, has been presented. A macerated fetus was delivered, but complete recovery of the mother occurred. After reviewing the literature it is believed that this is the first reported case in which both splenectomy and cesarean section have been performed.

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PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF DIABETES MELLITUS

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The purpose of this article is to present briefly certain concepts which the writers consider basically important in the management of uncomplicated diabetes mellitus. Most of the program to be discussed agrees in principle with teachings of recognized clinics on diabetes. There are, of course, variations in opinion concerning the details of management among various groups. Since diabetes is a common and chronic disorder of variable severity, and untreated diabetes is often compatible with life for long periods of time, these divergent opinions are understandable. The objectives of treatment remain the same with all groups, that is, maintenance of the patient in a good state of general health, and prevention of the occurrence of complications.

The pathologic physiology of diabetes mellitus is still a controversial subject involving intricate glandular interrelationships and the role of insulin in metabolic processes in body tissues, particularly in the liver and muscles. Brilliant contributions have been made but much remains to be done. From the practical standpoint the responsible disturbing factor may be considered a deficiency in the production of insulin with resultant hyperglycemia, glycosuria, tissue destruction with increased nitrogen excretion, a tendency to ketosis, acidosis, and coma, and a variety of well known symptoms whose number and severity differ with the severity of the disorder.

The diagnosis of diabetes mellitus as a clinical entity should be established with care. Not all examples of glycosuria and not all cases manifesting a decreased tolerance during the glucose tolerance test belong in this classification. Obviously, renal glycosuria may be misleading. A variety of endocrine disturbances and other disorders may be accompanied by a decreased tolerance to glucose, usually of mild degree, and often manifest only by the glucose tolerance curve. True diabetes may sometimes be present in these conditions, and distinction may then be possible only after treatment of the underlying process. Examples of these disorders include hyperthyroidism, Cushing's syndrome, acromegaly, and simple obesity. The finding of a blood glucose level of 130 mg. per cent or higher while fasting or two and one-half hours after a high carbohydrate meal, with or without glycosuria, is presumptive evidence of the presence of diabetes mellitus. However, the final diagnosis should be made only after a careful consideration of the factors just mentioned, since there is no conclusive evidence as yet that true diabetes mellitus is ever completely and permanently cured.

The criteria for adequacy of treatment generally and readily available are four: (1) the symptomatic response of the patient with all that this implies in control of classical symptoms, sense of well-being, growth and development in children, strength and normal nutritional status in adults; (2) the prevention of complications such as neuritis, retinopathy, vascular occlusion, and acidosis; (3) the prevention of glycosuria; (4) the maintenance of normal blood glucose levels. Other studies may be valuable during initial investigations but are not essential in evaluating diabetic control in the uncomplicated case.

It is often possible to maintain the patient in good nutritional balance and completely symptom-free in the presence of persistent hyperglycemia with resultant glycosuria. Since the mechanism of vascular damage in diabetes is not clearly understood, and since reports on the subject are somewhat conflicting, it is not possible to state with certainty that this lack of chemical control results in an earlier appearance of such damage.

However, because our yardsticks for the measurement of adequate treatment are few, yet simple and available to most practitioners, the writers feel that they should be utilized to the fullest possible extent. In other words, not only should the patient be healthy, but the level of glucose in the blood should be normal with a normal postprandial rise and subsequent fall, and glucose should be absent from the urine of those patients with normal renal threshold.

It is obvious that this ideal cannot be reached in all cases. It is, rather, a goal at which to aim, considering the age of the patient, the inherent instability of the diabetes, the frequency and severity of insulin reactions, the intelligent cooperation which may be expected, and other factors which may be apparent in the individual case. The occurrence of frequent insulin reactions would at first appear to be a serious objection to this routine. In actual practice, induced hypoglycemia in most diabetics has been infrequent and has not prevented the attainment of this type of control. It is, of course, far easier to maintain chemical control in older, more stable diabetics than in diabetic children and young adults. In these latter cases, normoglycemia is a goal to be sought, though rarely attained. As an ideal it is a stimulation to careful study and optimum regulation. Due consideration must be given at all times to growth requirements, nutritional requirements, and the avoidance of severe hypoglycemic episodes.

The more detailed summary of diabetic management will be discussed under the following headings: (1) initial study and regulation; (2) instruction of the patient; (3) diet; (4) insulin; (5) progress study.

Initial Study and Regulation

Having established the diagnosis and eliminated complicating factors by careful examination, including chest x-ray, examination of ocular fundi, and renal function tests in older patients, a period of daily observation is initiated for the purpose of diabetic regulation. This period may vary from a few days to two weeks or more, depending on the degree of severity and instability of the disease. During this time hospitalization is considered essential only for the patient whose diabetes is complicated by acidosis, gangrene, or serious systemic disease, or whose diabetes is so severe or unstable that ambulatory status is attended by grave risk. The average diabetic during the initial control period is encouraged in normal physical activity. He is seen once each day by the physician. Estimations of blood glucose levels are made two or three times each day before meals, that is, fasting and four hours and sometimes two hours postprandially. These are correlated with qualitative measurements of glucose in the urine, which is likewise collected before meals. With this routine of management, we find usually

that a single urine specimen before each meal is sufficient. In certain cases of severe and unstable diabetes, it is desirable to collect the urine output each twenty-four hours and to make accurate quantitative glucose determinations on each such sample.

These studies constitute a guide to the adjustment of insulin dosage when it is required or furnish an index to response when dietary management alone is sufficient.

During this time, also, the patient is instructed in measurement and manipulation of his diet, administration of insulin if needed, and all phases of diabetic management which are of importance to him. He is encouraged to devote his time entirely to the study of diabetes. At the expiration of the initial control period, it is expected that the diabetes will be sufficiently well stabilized to permit the patient to pursue his normal daily activities.

Instruction of the Patient

Successful management of diabetes mellitus is dependent as much upon the intelligent cooperation of the patient as upon any other single factor. Such cooperation can only be obtained from the patient who understands the necessity for the restrictions imposed upon him. The foundation of this understanding can be laid during the period of initial regulation. The fundamental alterations in his bodily physiology are simply explained. Potential dangers are stressed to emphasize the need for diabetic regulation, but he is assured that controlled diabetes is entirely compatible with good general health. He is taught to recognize the symptoms of acidosis or hypoglycemia, together with the appropriate steps to be taken in each. The necessity for added caution in the presence of infection or gastrointestinal disturbance is explained. Care of the feet is emphasized. Terms commonly used in discussing diabetes are defined and explained. Normal values for glucose in blood and urine are given. The technic for determination of glucose in the urine, using Benedict's qualitative reagent, is demonstrated. When insulin is necessary, its measurement and administration are explained and injections are given by the patient under supervision. The diet is verbally outlined, a printed list is furnished, and any dietary problems which may arise are discussed and settled. The patient is asked to obtain a diabetic manual and to continue his study of the disorder. Class instruction is indicated for groups of diabetics. Pertinent questions by the physician at the time of daily consultation during initial control will reveal the progress in learning made by the individual patient. The necessity for orderly living, regular habits, and avoidance of all excesses is emphasized. At all times

an effort is made to maintain morale at a high level by assuring the patient that diabetes, although inconvenient, is consistent with normal interests and activities. At the same time the fact is pointed out that he has a chronic disorder with which he must learn to live every day for an indefinite number of years and that the duration of life itself is dependent upon his full cooperation.

Diet

A rigid dietary program is fundamentally important in the successful management of diabetes. The above fact should be emphasized. Dietary instructions are troublesome and time-consuming. Without constant daily caloric and available glucose values, however, diabetic status will fluctuate widely, and consistent smooth regulation will not be obtained. For this reason we favor an exact, quantitative diet, even in the mild case. Accurate weighing of the dietary constituents is ideal and has a desirable psychologic effect. When practical, it should be used during initial dietary familiarization. A majority of patients, however, are well controlled on measured diets. The patient is thoroughly instructed in his diet during the period of initial control. Also during this period it is preferable, though not necessary, that the patient eat his meals in a dining room which is under the supervision of a skilled dietician. Obviously, such an arrangement is appropriate in large diabetic clinics; it is not a necessity, and the intelligent patient can follow a strict dietary program in his home environment during initial regulation.

It is not within the scope of this article to discuss the various types of diets which have been advocated and used in the management of diabetes. For a number of years we have used diets of relatively high carbohydrate, low fat content, with adequate maintenance amounts of protein. The importance of high protein intake should be emphasized. Our trend over a period of years has been to show an increasing quantity of this constituent in dietary prescriptions.

The caloric value of the diet usually depends upon the following considerations: (1) actual weight of the patient in comparison with the ideal weight for height, age, and sex; (2) growth requirements in the case of children; (3) anticipated physical activity. For practical purposes, basal caloric requirements for ideal weight based on height, age, and sex may be quickly determined from a slide rule.* The diet may be maintained below this level to promote weight reduction when such is indicated, or additional calories up to 100 per cent or more above basal caloric requirements may be necessary in the case of malnourished or very active individuals. In our experience, the average adult engaged in a sedentary occupation requires from 30 per cent to 50 per cent above

**The slide rule furnished by Eli Lilly and Co. is convenient and suitable for this purpose.*

the basal caloric requirement in order to maintain weight at or slightly below the calculated ideal level. These preliminary calculations constitute a convenient working basis but will be subject to modification as the patient's weight response is noted on subsequent examinations.

The important factor of normal growth requirements enters into the problem in diabetic children; here, the caloric requirements must be calculated on the basis of standard height and weight for age and sex. We have found the Baldwin-Wood charts convenient for obtaining these standards.

When diabetic management is initiated the diet prescription must be fitted to the individual case. For example, the patient of normal weight or less with mild diabetes may be started on his final calculated diet, and his response noted. However, the obese diabetic or any who may require insulin are started on a basic diet containing approximately 100 Gm. of carbohydrate, 62 Gm. of protein, and 50 Gm. of fat, a total of 1098 calories. Subsequent increases, when higher caloric values are indicated, are ordered by number, each numerical increase in carbohydrate and protein being equivalent to one slice of bread, a technic originally formulated by Rabinowitch. Increased caloric requirements are readily met by increasing the fat content of the diet. The carbohydrate to fat ratio in each case is usually kept at approximately 2 + :1. A sample of a portion of the diabetic order sheet will make this clear.

	Prescribed Diet					**Standard Diets**				
1946 Date	Diet No.	C	P	F	CAL.	Diet No.	C	P	F	CAL.
4-28	Basic	100	62	50	1098	Basic	100	62	50	1098
5-2	3+	145	71	70	1494	1	115	65	50	1170
5-5	5+	175	77	80	1728	2	130	68	50	1242
						3	145	71	50	1314
						4	160	74	50	1386
						5	175	77	50	1458
						6	190	80	50	1530
						7	205	83	50	1602
						8	220	86	50	1674
						9	235	89	50	1746

In the type of case just described, response in blood and urine glucose values to the basic diet is observed for several days, and insulin is started, if considered necessary, before any increase is made in the caloric value of the diet. Subsequent increases are made in several stages as indicated on the order sheet and the diabetic response noted to each before the final value is reached. When insulin is required, the dosage is adjusted and approximate diabetic control is obtained before the diet is increased from one level to the next. It then becomes comparatively simple to increase the insulin dosage to match the increased caloric value of the diet.

A sample menu based on the basic diet we use is as follows:

Weight (Grams)	Household Measurements	Grams CHO	Grams Protein	Grams Fat
	Breakfast			
	1 serving of fruit	10		
	1 egg		6	6
30	1 slice whole wheat bread	15	3	
5	½ square of butter			4.5
100	½ glassful of milk	5	3.3	4
	Coffee or tea as desired			
	Luncheon			
90	3 counces of meat or substitute		18	7.5
200	1 cupful cooked 5% vegetable	10	.2	
100	1 cupful raw 5% vegetable	5	1	
5	½ square of butter			4.5
	1 serving of fruit	10		
200	1 glassful of milk	10	6.6	8
	Dinner			
90	3 ounces of meat or substitute		18	7.5
200	1 cupful cooked 5% vegetable	10	2	
100	½ cupful 10% vegetable	10	1	
5	½ square of butter			4.5
	1 serving of fruit	10		
100	½ glassful of milk	5	3.3	4
	Total	**100**	**64.2**	**50.5**

A few explanatory statements are in order. It is apparent that the quantity of a serving of fruit and the weight of the serving must vary with the carbohydrate content of the fruit in order to furnish 10 Gm. of carbohydrate. For example, a serving of unsweetened applesauce is 6 tablespoons or 75 Gm., while a serving of cooked rhubarb is 1½ cupfuls or 300 Gm. Printed lists of fruits, cereals, 5 per cent, 10 per cent, 15 per cent, and 20 per cent vegetables, various substitutions, and foods of no caloric value are furnished to the patient. These values may be obtained in any standard text on dietetics. It should be apparent that carbohydrate, protein, and fat contents of the same type of food vary from day to day and that an analysis of an aliquot of a day's food would reveal values somewhat different from those given above. The analyses given in various texts also differ in some instances. However, for practical purposes in day by day diabetic management, these values are sufficiently accurate to be readily usable.

The distribution of available glucose in this diet is, in round numbers, 30 per cent at breakfast, 35 per cent at luncheon, and 35 per cent at dinner. Approximately this same distribution is maintained as the caloric value of the diet is increased to meet individual requirements. This distribution is suitable for the diabetic who needs no insulin, or whose requirement of protamine zinc insulin is less than 20 units.

When the requirement of protamine zinc insulin, administered before breakfast, surpasses this value, we have found it convenient to alter the distribution of available glucose to furnish 20 per cent at breakfast, 30 per cent at luncheon, 40 per cent at dinner, and 10 per cent as a bedtime feeding. Obviously, minor alterations in the distribution of available glucose can be made if the need for such is indicated by persistent hyperglycemia at the same time each day. In the case of patients who are subject to frequent insulin reactions associated with physical activity, the use of small feedings between meals is helpful.

The so-called "diabetic foods", except for unsweetened canned fruits and non-caloric gelatin products, are neither prescribed nor recommended.

Insulin

At the present time a detailed discussion of the use of insulin can be an extremely complex subject. A great variety of modified insulins have been used in clinical investigation in the United States and abroad. Promising results have been reported, particularly in the management of severe and unstable diabetes, where variations in the duration of action of insulin are especially necessary. General use of one or more of these preparations will probably be indicated in the future. For the

present, however, satisfactory regulation can be obtained in the majority of patients who require insulin by the use of insulin, U.S.P., and protamine zinc insulin, U.S.P. Only rarely do we modify the action of each type by administering them simultaneously in the same syringe. It should be stated, however, that some diabetic clinics follow this practice with satisfactory results.

There are no set rules by which one can establish the need for insulin in a given case or determine the probable insulin requirement. Each patient is an individual problem. The age of the patient, the severity of the diabetes, the response to diet regulation, the total caloric requirements, and the relative "sensitivity" to insulin are all important factors which bear on the question. Unless there is judged to be imminent danger of severe acidosis, it is usually advisable to observe the response of blood and urine glucose values to a basic diabetic diet for several days. Unless there is a prompt fall in these levels indicating further reduction to near normal values in the future, insulin is started.

When studies indicate only intermediate severity and fair stability of the diabetes, it is usually satisfactory to initiate insulin management with protamine zinc insulin. An original dose of 15 to 20 units with subsequent modification based on clinical response and caloric requirement is usually suitable. We have routinely administered protamine zinc insulin in a single daily dose before breakfast.

In the individual with severe and/or unstable diabetes, initial regulation is most conveniently initiated with insulin, U.S.P. Because of the relatively short duration of action, dosage can be quickly and readily manipulated.

The original dose given three times daily before meals and at bedtime, is kept small until the degree of responsiveness to insulin can be estimated. The amount is then increased, based on blood and urine glucose findings and increasing quantity of the diet, until satisfactory control is obtained. Protamine zinc insulin is then started, the initial dose being 80 per cent of the total daily requirement of "regular" insulin. The "regular" insulin is reduced in quantity or eliminated beginning with the bedtime dose, and ultimately withdrawn entirely, usually in two to three days. In many cases requiring more than 30 units of insulin per day better regulation of the diabetes is maintained by administering a small dose of "regular" insulin in addition to the daily protamine requirement. As mentioned previously, we do not oridinarily mix these insulins before administration nor give them simultaneously in the same syringe.

The exceptional case of unusual severity and instability may require

radical alterations from the program described. It is, however, applicable to the majority of diabetics.

Progress Study

It should be emphasized that the period of initial diabetic regulation is a time of daily observation, careful study, frequent blood and urine glucose determinations, and adjustment of diet and manipulation of insulin until satisfactory control is obtained.

At the expiration of this period, the patient is discharged to return to his daily work and routine. He is expected to understand thoroughly the diet, the administration of insulin, and all phases of the diabetic life which will be of practical importance to him. He is directed to keep a daily record of qualitative urine glucose values, at first four times each day (before meals and at bedtime) and to bring this record on return to his physician. He should be seen again at gradually lengthening intervals. On each return visit his progress is evaluated by history, examination, weight, and glucose levels in blood and urine. Alterations in diet and insulin are made when indicated. It is our opinion that each diabetic, after the condition is well stabilized, should be seen by his physician at least once every four months for the remainder of his life.

This brief outline of some phases of diabetic management is presented because it has proved workable in practice, even though it may entail additional trouble at times for both physician and patient. It is believed that the type of control obtained by this routine approaches physiologic normality by the crude measurements now available. There are many variations possible in the complicated problems of diabetic management, and routines and standards naturally vary among different groups and individuals. Diabetes is the subject of extensive laboratory and clinical investigation, and further progress can certainly be anticipated.

It is the conviction of the writers that well controlled and stabilized diabetes tends to improve gradually in status, even though it is never cured, and no amount of work and trouble is too great if this end can be attained.

Summary

Some practical considerations in the management of diabetes mellitus are briefly reviewed. The problem is approached by consideration of the following aspects: (1) initial study and regulation; (2) instruction of the patient; (3) diet; (4) insulin; (5) progress study.

The writers are greatly indebted to Miss Marian Buck for many helpful suggestions in preparing the discussion on dietary management.

"NERVOUSNESS"

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"Nervousness" is probably the most misused term in medicine. The adjective nervous, properly defined, means "pertaining to or composed of, nerves; having weak nerves; easily agitated; vigorous in style." Through common usage both physicians and laymen have by habit employed this word to denote a multitude of poorly defined and poorly differentiated subjective and objective situations. In obtaining psychiatric histories "nervousness" is used to connote anything from extremely mild degrees of restlessness to the most severe psychoses.

"Nervousness" far outnumbers any other presenting symptom encountered in a neuropsychiatric practice. If a statistical study were made of presenting or dominant symptoms in all fields of medicine, "nervousness" would be near the top of the list, if not far ahead of all others.

"Nervousness" is actually a symptom which is a response to physical disease or signifies an aberrant reaction to a situation or a combination of circumstances to which the person may be or has been subjected. Constitutional inclinations are often responsible for the reaction patterns that may be developed. The most benign types of responses to critical situations are only rarely encountered in medical practice, since most persons so affected achieve a satisfactory solution to their problems with a resultant abatement of symptoms in a minimum of time. However, similar circumstances imposed upon a person having different constitutional tendencies might create a clinical picture severe enough to warrant medical attention.

It should be remembered that "nervousness" is frequently a genuine part or concomitant of physical diseases. The anxiety, apprehension, tension, and tremor seen in the most severe anxiety states are rarely as marked as those observed in a well defined hyperthyroidism. The lassitude, mental depression, and fatigability associated with post-malarial, post-influenzal, and dengue fever are often as pronounced as those experienced in the true endogenous depressions. Rarely does a physical disorder, especially that having reached chronicity, fail to present some anxiety, apprehension, tension, or disturbance in sleep rhythm. As these symptoms become manifest, they should be dealt with just as promptly as complications of other types. It may only take a few moments to reassure or encourage such a patient at the onset of this trouble, whereas, if permitted to go unnoticed for weeks or months, the successful treatment of these complications may require many hours of intensive work.

Never does a day pass in the life of a physician that he does not encounter a functional problem. The current medical periodicals contain many articles concerning psychosomatic problems. Psychiatrists revel in the belief that they have discovered something new in this fashionable term, "psychosomatic". In writing on the *Psychosomatic Aspects of Allergy* Karnosh has aptly referred to this condition: "In some respects, this new branch of medicine is a little presumptuous because it purports to demonstrate something new, when actually, a good deal of it is merely 'new cackling over an old egg'."

The family physician is in a most opportune position to deal with such problems. Having ministered to the family from the medical standpoint and as an advisor, he has knowledge or facts which frequently consume hours for a psychiatrist to obtain. Many patients confronted with emotional conflicts seek only an understanding ear, some sound advice, and judicious use of medication to gain relief from their illness.

At present I have under treatment a woman who has an anxiety state produced by an untenable domestic situation of years' duration. I regret that after several hours of interviews and psychiatric treatment she stated that her physician was no longer interested once she became "nervous". This particular problem does not involve any deep-seated psychological barriers and could be adequately dealt with by any competent physician, providing he gave the patient sufficient time to relate her story.

Psychoneuroses, whether they be major or minor, are nosologic entities having definite causative bases. Unfortunately it has become too common a practice to denote as a neurotic disorder a series or group of somatic symptoms for which there is no apparent physical basis. Once the condition has been labeled a functional disorder or a psychoneurosis, it too frequently ceases to be a therapeutic problem or to hold further interest as a diagnostic enigma. After the clinical entity is placed in such a category, the physician's next move often consists of nothing more than telling the patient not to worry about it, "forget it!", administering sedation, mild suggestion, and reassurance. No surgeon would consider that acute appendicitis had been adequately treated by merely giving aspirin, applying palliative measures to the external surface of the abdomen, and suggesting to the patient that recovery would result, nor would the internist treat pneumonia by administering analgesics, cough syrup, and reassurance. In the same light, it is incorrect to stop in the treatment of neuroses without ferreting out "the area of acute infection", which might consist of any one of a multitude of emotional conflicts, financial worry, maladjustments in life or occupation, marital or domestic discord, or sexual incompatabilities.

In dealing with the neuroses, it is well to remember that, as in treating neoplasms, there are benign and malignant conditions. The benign neuroses readily lend themselves to the various therapeutic technics at our disposal. Many of the psychoneuroses of long standing and of "deep-seated origin" can be classified as malignant.

In this latter group, after the psychiatrist has employed all the tools at his disposal without relief, or determines that the condition is "inoperable", one can expect only temporary relief from periodic mental catharsis on the part of the patient, and reassurance from the physician. It may be comparable to giving morphine to relieve the pain of a metastatic tumor.

The treatment of the psychoneuroses is, in general, about as poorly conducted as the condition is poorly understood. Common practice for years has been to give the patient a bottle of sedative, preferably bromide, and to tell him to "go home and forget it or take a nice, long rest." Fortunately, in a number of cases, this routine produces results because, as in general medicine, many pathologic situations of a mild degree will right themselves in spite of any measures that we physicians employ.

Sedation and hypnotics have, in general, been badly mishandled in the treatment of the functional disorders. The natural desire and expectation of the patient upon consulting his physician is to come out with a bottle of medicine or pills. It is indeed unfortunate that in dealing with the neuroses we have no specific. Many times the patient is led to believe or infers that medication which is actually meant to serve as an aid is being given to cure his nervous ills. It should be common practice, except in rare instances, that the physician, in administering a sedative to a neurotic, should definitely inform the patient that the preparation is being given only to allay some of his tension or improve his sleep. This admonition would prevent many obstacles that arise during psychiatric investigation and treatment. The patient is often reluctant to accept a psychogenic explanation after having received a bottle of "red medicine or white pills" for a period of months. His response is, "I must have something wrong physically or the doctor wouldn't have given me all that medicine!"

A few words regarding prolonged and excessive use of sedatives, chiefly bromides, are not amiss. Bromide intoxication is more common than most of us realize. When the insomnia, tension, weakness, headache, and other symptoms of a neurosis fail to respond to a short period of bromide administration, more of the same preparation is frequently ordered. This may accentuate the original symptoms and produce new and more serious complications. Skin eruptions, irritability, mental con-

fusion, speech and gait disturbances, memory defect, stupor, and evidence of dissociation often become manifest. It behooves all of us to be ever alert for indications of bromidism. Clearing of mental symptoms due to this cause may not be distinguishable for at least two to three weeks following the return of the blood bromide level to normal.

In selected cases, rest is advisable, but on the whole it is a most abused form of treatment in psychiatric disorders. Weir Mitchell influenced the thought in medicine for many years by his teaching that nervous illness was the result of physical exhaustion, and as such required complete bed rest, complete isolation, no letters, reading, or writing, and constant attendance of a nurse. Present day psychiatric teaching considers this form of therapy to be incorrect. The easy fatigability of the neurotic is a symptom of his disorder and not an entity in itself. The cure of the neurosis depends on the removal of the factors that cause the individual to deplete his strength and the direction of his energies into gainful or amusing channels. Occupational therapy is one of the most valuable methods by which such an end is attained.

The successful treatment of psychiatric illness, particularly the psychoneuroses, rests in determination and correction of the etiologic factors. This is accomplished by various types of psychotherapy which have been developed throughout the years. Volumes have been written on psychotherapy, but, to my knowledge, nowhere is there recorded a clear, concise routine of treatment such as may be employed in medical and surgical diseases.

The reason becomes obvious when we consider that we are dealing with personalities, as varied as anything in the universe, on the part of both patient and therapist. Direct questions and answers suffice in some problems, while in others it becomes essential for the psychiatrist to "tease out" the emotional conflicts by having the patient relate the facts as he wishes.

Hypnosis, true or induced by drugs, is a valuable implement in the armamentarium of the present day psychiatrist. Grinker and his associates had success in treating combat neuroses by narco-synthesis. This procedure employs analysis of causative factors, suggestion, and beginning re-synthesis of the personality while the patient is under the influence of an hypnotic drug.

Psychoanalysis typifies psychiatry to many a layman. Every psychiatrist has been asked, professionally and socially, if he would analyze the inquisitor, the assumption being that such a procedure is easily accomplished within a few minutes. Actually, psychoanalysis is a time consuming measure and dangerous unless properly conducted. As such its scope is limited and should be applied only in carefully selected cases.

"Nervousness" is a symptom which may be part of organic disease, or it may constitute the subjective and objective manifestations of functional problems. By necessity, only the latter concepts were touched upon during this discussion. "Nervousness" is not imaginary, as many believe, nor volitional, but a disturbance in re-activity, whether it be overt or implicit. Probably all such symptoms are mediated at subconscious levels and may or may not present physiologic changes of the nervous system, particularly the sympathetic.

Psychiatry is dynamic, consequently the approach to any psychiatric disorder cannot be concerned merely with an analysis of that particular isolated phase in the patient's life. To gain full understanding, longitudinal study must be carried out. Psychiatry is no longer in the realm of the mystic or supernatural.

PAIN AND FEVER ARISING FROM THE COMMON BILE DUCT AND NOT ASSOCIATED WITH JAUNDICE

Report of 2 Cases of Choledocholithiasis Treated by Choledochostomy and 1 of Post-Cholecystectomy Biliary Dyskinesia Relieved by Vagotomy.

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Division of Surgery

When biliary colic, chills, or fever persist in a patient who has had a cholecystectomy for gall stones, the presence of a calculus in the common bile duct is often suspected. Yet, in the absence of stones in the gall bladder, it is only rarely that stones in the common duct produce these symptoms without causing sufficient obstruction to result in jaundice.

It is the purpose of this article to call attention to the fact that stones in the common duct may produce pain or fever without jaundice and to report 2 illustrative cases. A case of postoperative biliary dyskinesia relieved by vagotomy is also reported.

Case Reports

Case 1. Chills and fever without jaundice caused by a stone in the common duct. A 62-year-old white woman was admitted to the hospital complaining of chills and fever of 105° which had occurred approximately once a week for eighteen months.

The attacks were accompanied by vomiting and vague upper abdominal distress, at times radiating to the back.

The only pertinent disclosure in her previous history was a cholecystectomy done sixteen years before for cholelithiasis. This patient had undergone extensive examination at another hospital, and a tentative diagnosis of undulant fever had been suggested. Undulant fever skin test and agglutination at Cleveland Clinic Hospital were negative, as were smears for malaria. Blood cultures, gastrointestinal x-rays, intravenous urogram, cystoscopy, and retrograde pyelogram were all negative. Icteric index was 7. There was no history of jaundice, and no jaundice followed the chills and fever observed during the patient's stay in the hospital (fig. 1).

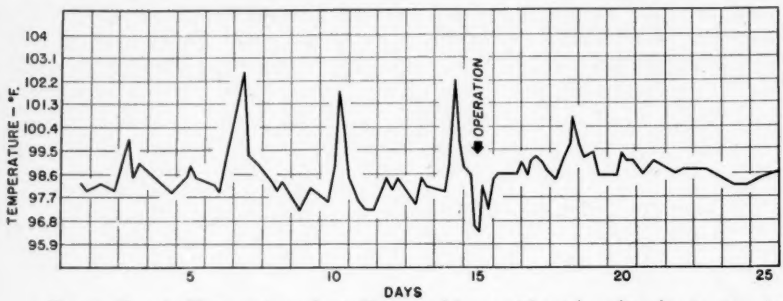

FIG. 1. Case 1. Temperature chart. Chills and fever without jaundice due to stone in common duct.

FIG. 2. Case 1. Stone removed from common duct.

On the basis of a palpable enlargement of the liver and a history of cholecystectomy for gall stones, the possibility of a common duct stone was considered and operation advised. At operation, the common bile duct was found to be enormously dilated to a diameter of 1½ inches. It contained a single round stone the size of a large olive (fig. 2). There was complete relief of symptoms following choledochotomy and removal of the stone.

Case 2. Biliary colic without jaundice caused by multiple stones in common duct. A 69-year-old white woman was admitted to the hospital with the chief complaint

of abdominal pain. She gave a history of cholecystostomy with removal of stones from the gall bladder nine years before. She had experienced mild abdominal pain several times since. Two months before admission she had suffered colicky pain in the epigastrium and right upper quadrant with radiation to both sides and to the angle of the right scapula.

These attacks were accompanied by bloating and belching and occurred almost daily fifteen to twenty minutes after meals. They were aggravated or precipitated by ingestion of greasy or fried foods and were relieved by induced vomiting. The patient had had no chills, fever, or jaundice, and no light stools.

Physicial examination revealed no icterus. There was mild guarding in the right upper quadrant and enlargement of the liver two fingers' breadth below the costal margin. The pertinent laboratory findings were: icteric index 10, cephalin cholesterol flocculation plus minus, bromsulphalein retention 32 per cent after thirty minutes, and prothrombin time fifteen seconds. A surgical consultation was requested, and on the basis of the enlarged liver, colicky pain, and history of cholecystostomy for stones, operation was advised.

At operation the gall bladder contained no stones. There were seven faceted stones about 1 cm. in diameter in the common bile duct. Again there was complete relief of symptoms following choledochotomy and removal of stones.

Case 3. Post-cholecystectomy biliary dyskinesia relieved by subdiaphragmatic vagotomy. A 45-year-old white man was seen at Cleveland Clinic complaining of "pain in the liver." He had had a cholecystostomy for stones eighteen years previously, and a cholecystectomy thirteen years before. Since the last operation he had had a great deal of pain in the right upper quadrant, radiating around the costal margin and to the back. The pain was often nocturnal, having no relation to meals. Baking soda sometimes gave temporary relief. He had had no chills, fever, or jaundice. The patient's symptoms were so severe that he was well only about one week out of four and was unable to work.

The only positive laboratory findings were deformity of the duodenal bulb and spastic colon. He was placed on ulcer and bowel management. For the next four years he was seen at regular intervals. His symptoms continued, and at no time was he completely relieved by medical management. No ulcer crater was demonstrated, although the deformity of the duodenal bulb was seen repeatedly. Finally, due to the continuation of symptoms, he was referred for surgical opinion, and operation was advised. Two possibilities were considered—peptic ulcer and stone in the common duct.

At operation no ulcer was found, and there was no scar suggesting a healed ulcer. The common bile duct was not dilated, and no stones could be palpated. It was found that adhesions from previous operations caused the duodenal deformity. A subdiaphragmatic vagotomy was performed in the hope of relieving the biliary dyskinesia. It is now five months since operation, and the patient has had complete relief.

Review of Literature and Analysis of Cases

A review of 50 recent cases of choledocholithiasis proved at operation at Cleveland Clinic reveals no patient who, in the absence of stones in the gall bladder and in the absence of jaundice, had experienced chills, fever, or colic from stones in the common bile duct.

In these 50 cases there were 5 with stones in the common duct without jaundice, but these all had an associated cholelithiasis. A tabulation of symptomatology in these cases of choledocholithiasis is included.

Leading symptomatology in 50 cases of choledocholithiasis:

Biliary colic	92%
Jaundice	90%
Vomiting	46%
Chills and fever	40%

In our cases of choledocholithiasis not associated with stones in the gall bladder there was a slightly higher rate (10 per cent) than is usually reported. Reports from Mayo Clinic show 6.4 per cent, Lahey states that 4 per cent have common duct stones without cholelithiasis, and Cole agrees that the incidence is less than 5 per cent.

The incidence of choledocholithiasis without jaundice is given as 34 per cent, 15 per cent, and 39 per cent by Allen, Kerr, and Lahey, respectively. Although it is not uncommon for stones to be present in the common duct and give no symptoms, it is unusual for stones that do not cause sufficient obstruction to produce jaundice to give any symptoms. We have found only 1 report of a similar case, reported by O'Shea in a review of 2602 cases.

The number of patients who have had gall bladder surgery but continue to have biliary disease is startling. In a review of 485 cases Carter and Maraffino found that 193 had recurrent symptoms, 16 per cent of whom required further surgery. Trueman reviewed the cases in which operations for biliary disease had been performed at Mayo Clinic and found that 29.6 per cent had had previous biliary surgery. The occurrence of distress postoperatively has been variously attributed to retained calculi, re-formation of stones, expulsion of stones through the biliary tract, pancreatitis, sphincteritis, hepatitis, stricture of the papilla of Vater by injury from a stone, and spasm of the sphincter of Oddi, or biliary dyskinesia.

Whatever its cause, if postoperative pain occurs without jaundice, many surgeons hesitate to advise further surgery. They are inclined to consider the manifestation as functional or to attribute it to dyskinesia rather than to the presence of a stone in the common duct. Lahey has said that one of the most difficult decisions to make is to determine whether or not operation should be performed on an unjaundiced patient who has had a cholecystectomy for stones but still has pain. Too often surgeons have opened the common duct for just such symptoms and found nothing to explain them. Walters, on the other hand, emphasizes the fact that a stone in the common duct should be suspected in the presence of abdominal pain, nausea, and vomiting, even in the absence of chills, fever, and jaundice. Graham and Mackey have rightly emphasized the fact that if stones were not found in the gall bladder at the

first operation there was a greater chance of persistence of symptoms postoperatively without organic basis.

Discussion

It is conceded that exploratory operations after cholecystectomy performed for biliary colic without jaundice are unsatisfactory and that, in most cases, no gross abnormality is found. In such cases the surgeon is forced to content himself with draining the common duct. However, the 3 cases reported are examples of the positive results which render operation advisable in certain cases.

The first 2 cases are unusual, not because large or numerous stones occurred in the common bile duct without causing jaundice, but rather because in the absence of stones in the gall bladder, the common duct stone caused chills and fever in the first case, and in the second severe colic unaccompanied by jaundice. If there had been stones in the gall bladder to which the symptoms could have been attributed, the absence of jaundice would not have been noteworthy, since approximately 25 per cent of all common duct stones occur in patients who give no history of jaundice. In the majority of cases in which there are common duct stones without jaundice, however, it is probable that the pain is caused by the stones in the gall bladder rather than by the stones in the common duct. Colic or fever secondary to stones in the common duct is usually accompanied by sufficient obstruction to cause jaundice.

These 2 cases represent the only instances in the last 50 cases of proved choledocholithiasis seen at Cleveland Clinic in which, in the absence of stones in the gall bladder, stones in the common duct have caused fever or colic without jaundice.

The third case is noteworthy because of the dramatic relief of symptoms following subdiaphragmatic vagotomy in the case of a patient who had been totally incapacitated for work by severe and frequent attacks of pain in the epigastrium and right upper quadrant in the absence of any demonstrable lesion of the biliary tract. This operation, recommended by Dragstedt for the treatment of peptic ulcer, is safe and simple, and although no conclusion can be drawn from a single observation, it would seem worth trying when confronted with the problem of intractable biliary colic and a grossly normal common bile duct.

Many patients who experience a persistence or recurrence of biliary colic following cholecystectomy but give no history of jaundice are highly emotional women. This type of patient is usually classified as "neurotic", and in many cases this designation is justified. Yet the work of McGowen, Butsch, Walters, and others who have studied this problem indicates that there is an element of spasm and increased pressure in the duct

associated with the attacks of pain. Whether section of the vagus nerve below the diaphragm will consistently accomplish what denervation of the common duct and section of the splanchnic nerves have failed to do requires much more evidence than is afforded by a short study of a single case.

Summary

1. Stones in the common duct, when not associated with stones in the gall bladder, rarely cause chills, fever, or pain without causing jaundice.

2. Two cases are reported in which there were no stones in the gall bladder, but in which stones were present in the common duct without causing jaundice. In the first case a single large stone caused chills and fever for a year and a half. In the second, stones in the common duct caused severe biliary colic.

3. Persistent or recurrent pain following cholecystectomy may be due to stones in the common bile duct, but in the absence of jaundice this is unusual.

4. A case of post-cholecystectomy biliary dyskinesia relieved by subdiaphragmatic vagotomy is reported.

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THE CONTROL OF HEMORRHAGE IN OTOLARYNGOLOGY

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Hemorrhage from any part of the body is distressing and terrifying to the patient. In the field of otolaryngology this is particularly true, for the patient has not only the fear of bleeding to death but also the fear of suffocation from the accumulated blood. This fear arises because the bleeding most often fills the air passages, interfering materially with breathing.

Severe hemorrhage from the ear is rare but can occur. It may follow trauma which has ruptured the ear drum or caused a skull fracture through the temporal bone. These hemorrhages are usually not severe and should be left alone. Ear drops should never be used in such cases unless infection ensues. If there is no infection the use of irrigation or the instillation of drops may set up a serious infection.

Blood may collect in the tympanum behind an intact drum following neurosurgical procedures in which the cranium is opened close to the mastoid and some of the mastoid cells exposed. Blood may also reach

the tympanum during a severe nasal hemorrhage, the blood flowing up the eustachian tube. In both these situations one usually treats the condition expectantly.

In the former an attempt to evacuate the blood by myringotomy and inflation might lead to intracranial infection, and in the latter one can do no intranasal manipulation other than that required to stop the nasal hemorrhage.

Severe hemorrhage can occur in the following instances:

1. After myringotomy in a patient with a high jugular bulb extending into the lower part of the tympanum. Such an anomaly is rare, but when it exists the drum may have a bluish cast. It is safer not to incise this type of drum.

2. Postoperatively following a mastoidectomy when there has been a surgical or pathologic exposure of the lateral sinus. Severe hemorrhage from the canal in this situation may mean rupture of the lateral sinus. The wound should be opened quickly, and the surgeon should be prepared to pack off the lateral sinus if this proves to be the source of the bleeding.

One patient with such symptoms was a child who had had a simple mastoid operation disclosing a large pathologic exposure of the lateral sinus. Since the perforation in the drum had been inadequate, a myringotomy had also been done. That evening a rapidly enlarging spot of blood appeared on the bandage. The child was taken to the operating room immediately and the bandage was removed under ether anesthesia. Active bleeding was coming from the canal, but none from the mastoid wound. No blood was found in the mastoid cavity, and the sinus was intact. The bleeding came from the drum, and a pack in the external canal controlled it easily. Yet, in similar cases the physician should not neglect inspection of the mastoid cavity and the lateral sinus.

3. Another serious type of hemorrhage from the auditory canal is that associated with an infection in the lateral pharyngeal space. This indicates a ruptured internal carotid artery, and ligation of the common carotid artery should be done at once to prevent a fatal outcome.

Nose bleeds are usually thought to be of minor consequence, but a severe nasal hemorrhage can be one of the most harrowing experiences in the practice of otolaryngology. The simple epistaxis usually receives no more attention than the old-fashioned home remedies of cold water and cold cloths, folded paper placed under the upper lip, or a cold metal key hung down the back between the shoulder blades.

When severe nasal hemorrhage occurs the blood may pour out so rapidly that examination of the nasal cavity may be almost impossible. When it stops the source of bleeding may be difficult to locate. A de-

termined effort should be made to locate the bleeding point and cauterize the ruptured vessel. If the bleeding is brisk it may be slowed by temporarily placing adrenalin packs in the nose. It is well to mix some 10 per cent cocaine with the adrenalin so that some measure of anesthesia is obtained. A suction tip may remove the blood rapidly enough to trace the source of bleeding. A small blood clot in the ruptured vessel wall may extrude as a raised red or white dot on the surface of the mucosa, and if this is displaced during the removal of clots, bleeding may recur slowly or even briskly. The bleeding must be stopped and the area cauterized after reinsertion of an adrenalin and cocaine pack against the bleeding point.

If the vessel is relatively small the application of a 50 per cent solution of trichloracetic acid may control it. A cotton-tipped probe is dipped into the solution and the adrenalin pack gradually pushed back until the tip of the probe is in contact with the bleeding point. If the vessel is large, electrocoagulation must be done under complete local anesthesia or under general anesthesia with pentothal sodium.

Fortunately most nasal hemorrhages originate in Kiesselbach's or Little's area on the septum. This area is easily accessible for inspection, packing, and cauterization. Figure 1 shows the distribution of the major vessels over the septum. The blood vessels in this area are arranged in the form of a plexus and are more susceptible to trauma than the rest of the nose. The blood vessels of the nasal cavity may dilate and contract quite rapidly and to a marked degree.

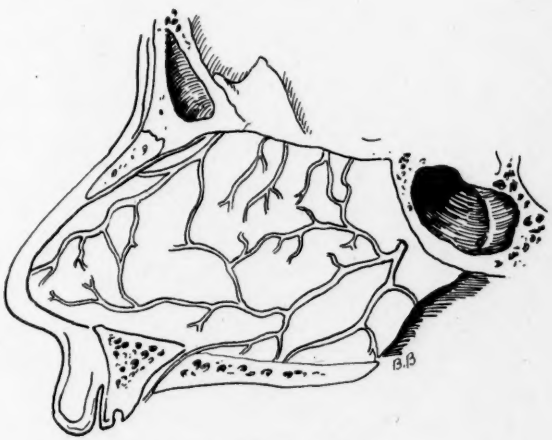

FIG. 1. Blood vessels of septum.

One patient gave the history of severe nose bleeds, but at the time of examination there was nothing to be seen in the nasal cavity. She was told to return while the nose was bleeding, and before she left the building the epistaxis recurred. A ruptured dilated vessel about a millimeter in diameter was seen in Little's area. These vessels may be made to dilate by spraying them forcibly with a 2 to 4 per cent cocaine solution. This procedure may also wash off small blood clots and start slight bleeding from the area being sought.

Nasal hemorrhage, difficult to visualize and difficult to control, may occur from larger vessels high up on the septum or back in the nasal cavity.

Figure 2 shows the distribution on the lateral wall of the nose. Bleeding coming from beneath the turbinates, frequently beneath the posterior end of the inferior turbinate, is also difficult to control even with packing.

When the hemorrhage is severe and the bleeding point cannot be seen, it is best to pack the nose tightly to prevent further loss of blood. For this, softly rolled cotton packs about the size of one's little finger and long enough to reach the entire length of the nasal cavity are preferred. They may be moistened with some preparation like thromboplastin. The first pack is placed on the floor so that one end reaches the posterior naris and the other the vestibule. It is then pressed down on

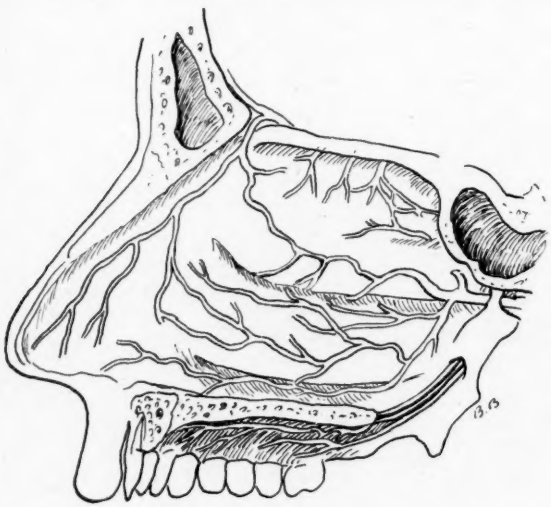

FIG. 2. Blood vessels of lateral wall of nose.

the floor and pushed laterally under the inferior turbinate. The second pack is pressed down on top and medial to the first. In this way packs are placed on top of each other until the entire cavity is tightly packed. If bleeding still continues the forceps may be worked between the central packs and then spread so that the upper packs are forced higher into the cavity. In this way another pack may be inserted. The number of packs must be recorded since they are left in the nose for two or three days. They may be removed one a day if desired. It is seldom necessary to use a postnasal pack when the nasal cavity has been treated in this fashion.

If bleeding recurs upon removal of the packs, the nose can be repacked. However, if packs are left in the nose too long the membranes become macerated, and new bleeding points occur when they are removed.

A more direct method of permanent control is electrocoagulation. After the severe hemorrhage is controlled or at least slowed by the packs, the patient can be placed under general anesthesia with pentothal. A postnasal tampon is pulled into place through the unpacked side. The nasal packs are then removed from the involved side and search made for the source of bleeding. A metal suction tip is covered with a sheath of rubber tubing, leaving the metal tip and the handle exposed. With this instrument one can remove the blood and follow it to its source. The electrode of a coagulating diathermy machine is then placed against the handle of the suction tip and the bleeding point coagulated until bleeding ceases. The suction keeps the field dry enough for the current to act on the desired point. It may be necessary to use adrenalin packs and pressure first in order to slow the bleeding sufficiently for the above procedure.

Local causes for the nasal hemorrhage must be sought. There may be a malignant neoplasm in the nasal cavity which is easily found and readily recognized. A biopsy will establish the correct diagnosis, and proper treatment can be instituted. A badly deviated septum is sometimes responsible for sufficient distortion of the blood vessels to make them prone to rupture. A badly deviated septum may also prevent proper access to the posterior nasal chamber. In either of these conditions a submucous resection is indicated.

One relatively young hypertensive patient had recurring extremely severe nasal hemorrhages over a period of many years. In one recent attack it was found that a badly deviated septum prevented good access to the posterior portion of the right nasal cavity, the side which produced the hemorrhages.

She was having a very severe hemorrhage, and when the right side was packed blood poured out the left side. The left side was packed and blood ran out the eustachian tube. It also ran up the nasolacrimal ducts and into the eyes. It finally was brought under control, and eventually the packs were completely removed. The nasal cavity could not be searched because of the septal deviation.

Two years later the patient returned with a somewhat less severe hemorrhage which was more easily controlled. This time she would not leave the hospital until the submucous resection was done. After the deviation was removed a small hemangioma was found on the septal membrane high up and just behind the sharp edge of the deviation on the right side. The hemangioma was cauterized.

Hemorrhage has been reported as originating in the antrum without fracture or infection.[1] Only a thickened membrane was found in those cases where a Caldwell-Luc operation had to be done to control the bleeding. Many of these cases were controlled by several irrigations alone and without operative interference.

In severe bleeding following intranasal operations the source of bleeding may be traced and controlled by electrocoagulation. The type of operation often indicates the source of bleeding. After spheno-ethmoid evisceration, for example, one should look for bleeding from the sphenopalatine artery at or just below the operative opening into the sphenoid. The anterior or posterior ethmoid arteries may be the source of the bleeding. Intranasal packing may be required.

Transantral ligation of the internal maxillary artery in the sphenomaxillary fossa has been successfully done in many severe nasal hemorrhages.[2]

This provides positive control of bleeding from one of the branches of this artery. It is not a simple procedure but must be seriously considered in those cases of intractable nasal hemorrhage which refuse to yield to more conservative measures.

In all severe nasal hemorrhage cases a complete medical examination should be made. This is particularly necessary when bleeding tends to recur. The great majority of these patients will be found to be hypertensives, for which condition they require treatment. Sometimes hemorrhagic disease which needs attention may be found.

One disease in which there may be hemorrhages, not only from the nose but also from other mucous membranes, even the skin, is hereditary hemorrhagic telangiectasia, or Osler's disease. The hemorrhages occur most frequently from the nose. Often several members of the family will have the condition. There are many small telangiectasias scattered through the mucosa of the nasal cavity and mouth and in the skin. The

bleeding lesions can be cauterized, or, if too numerous, can be treated with radium. More than one radium treatment is usually necessary.

Hemorrhage from the nasopharynx may result from the presence of hemangioma, nasopharyngeal fibroma, or malignant disease. It may follow adenoidectomy or result from infection in the lateral pharyngeal space with rupture of the internal carotid. Following adenoidectomy hemorrhage can usually be avoided by careful hemostasis in the operating room. Tabs of adenoid tissue which may continue to bleed should be located and removed. Occasionally a bleeding vessel which requires clamping with a hemostat and tying may be present. If the hemorrhage cannot be controlled in any other way, a postnasal tampon is inserted. Hemorrhage from a nasopharyngeal fibroma can be avoided by recognition of the tumor and treatment with radium, which will cause enough fibrosis of the many blood vessels to simplify excision. Attempts to remove these fibromata without preliminary irradiation can result in serious hemorrhage.

Throat conditions which must be considered are hemangiomata, other neoplasms, and the effects of previous operations. Severe bleeding may occur during the course of a tonsillectomy. Deaths have been reported from the rupture of an anomalous internal carotid artery displaced to the region of the posterior pillar. As a rule severe bleeding in tonsillectomy can be avoided by keeping the dissection close to the surgical capsule, and ligating carefully all bleeders. A search of the fossa may reveal rather large veins that have been severed and the ends sealed off so that they are not bleeding at the time. These should be clamped and tied. It is better to eliminate completely all potential bleeders at operation while the patient is well anesthetized.

Even with great care, a few patients will have postoperative hemorrhages within the first twelve to twenty-four hours. This type of hemorrhage is usually from a vessel that was not ligated or one from which the ligature has slipped. Before leaving the operating room the patient should be warned not to suck on his throat or clear it for several hours. If bleeding does occur the vessel must be located and ligated. The reinjection of novacaine and adrenalin in the bleeding area will help control it and provide anesthesia for the clamping and ligating. Occasionally it is a general ooze which can be controlled by pressure with a gauze sponge or by removal of a poorly formed clot.

Delayed hemorrhage may occur on the fifth to the seventh day after tonsillectomy. These are seldom severe, but they frighten the patient. Removal of the clot and pressure with a sponge are usually sufficient. If the bleeding has stopped and there is a well formed clot, it may be left alone. It is usually best to hospitalize such a patient for observa-

tion. Small doses of morphine will frequently quiet him enough to stop the bleeding. These postoperative hemorrhages are the result of separation of a slough in the tonsillar fossa and are usually seen in patients who have failed to keep the throat clean and in whom there is considerable secondary infection.

The most serious hemorrhage—that with the highest and swiftest mortality—may occur during the course of infection in the lateral pharyngeal space (figure 3). It may follow a tonsillitis, a peritonsillar abscess, or a retropharyngeal abscess with extension into this space. It is most often the result of infection, rupture, and false aneurism of the internal carotid artery. The rush of blood is held in check for a time by

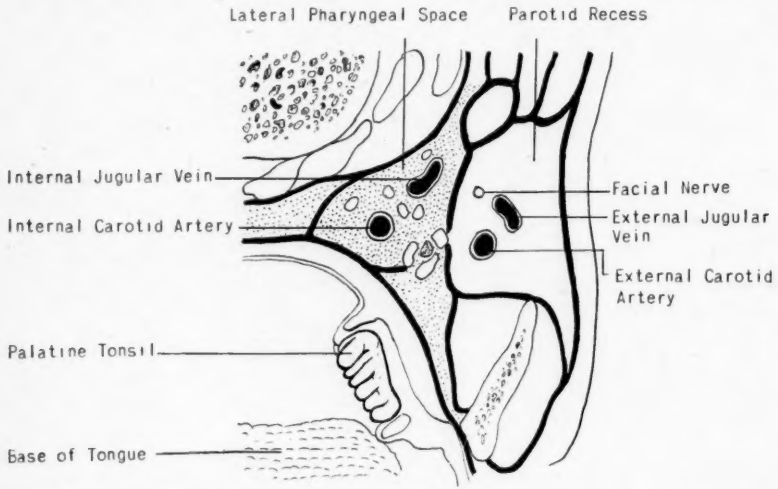

FIG. 3. Lateral pharyngeal spaces.

the walls of the abscess cavity. It may burrow and rupture into the external auditory canal with a severe hemorrhage from that orifice. It may also burrow upward and rupture into the nasopharynx above the soft palate. The peritonsillar or retropharyngeal abscess may be incised, thus weakening the confining walls of the false aneruism. If such an abscess yields no pus but only some dark blood, one should be on guard for severe hemorrhage. A single fulminating hemorrhage has resulted in death before anything could be done.

If there is evidence of infection of the lateral pharyngeal space and severe hemorrhage from the ear, nasopharynx, or pharynx occurs, the patient should be taken to the operating room immediately and the

common carotid artery ligated. Delay may result in a second and possibly fatal hemorrhage.

The external carotid artery has been the site of rupture in a few cases, but the internal carotid is by far the one most frequently affected. Since most of these cases occur in children, serious intracranial complications are relatively infrequent as the result of sudden ligation of the internal carotid artery. But even with the possibility of such an occurrence one must act quickly, for to temporize means death. Fortunately these cases are uncommon, yet Salinger and Perlman collected 231 in their report in 1933.[3] Every physician should be familiar with this condition because when suddenly confronted with such a case he does not have time to study the literature. It is to be hoped that present day chemotherapy will halt such infections before they have created such serious damage.

Bleeding from the mouth may have its source in the mouth itself, the posterior portion of the nose, nasopharynx, pharynx, esophagus, or tracheobronchial tree. The patient's account of the occurrence is seldom helpful in tracing the source of the bleeding. When the bleeding arises from the posterior part of the nose or nasopharynx, some blood often comes from the nose; when it arises from the esophagus there is often vomiting and tarry stools, and when from the tracheobronchial tree, there is usually a cough which raises old blood and clots after active bleeding has subsided.

Careful examination with postnasal and laryngeal mirrors and nasopharyngoscope may reveal the lesion responsible or may trace the source of the bleeding. If blood is seen below the vocal cords the search must be continued with the bronchoscope.

When the esophagus is suspected, it is first studied with the fluoroscope, and roentgenograms are taken. This is followed by esophagoscopy. The lesions which may produce bleeding are varicose veins, malignant neoplasm, peptic ulcer of the esophagus, and the presence of a foreign body. The history and the roentgen examination will usually reveal the nature of the lesion.

In esophageal varices there may be no history of dysphagia. The first intimation of such involvement may be a massive hematemesis or massive gastrointestinal bleeding with tarry stools. Treatment consists of repeated injections of a 5 per cent solution of sodium morrhuate through the esophagoscope with an especially designed needle. As much as 9 cc. of the solution has been injected by Moersch at one treatment, but he advises using smaller amounts in most cases.[4]

In carcinoma of the esophagus there is a history of progressive dysphagia over a period of less than a year. At first there is difficulty

with the swallowing of solid foods and later with liquids. When the neoplasm is not too large and involves either the upper or lower end of the esophagus, surgical removal may be successful. If the carcinoma is found in the midesophagus, the problem is greatly complicated. Some successful removals have been reported. Irradiation therapy has been disappointing.

A neglected foreign body may result in fatal massive hemorrhage from perforation into the descending aorta.

One patient, a 14-year-old girl, swallowed a chicken bone which lodged crosswise in the esophagus. She was given bread and mashed potatoes in an attempt to dislodge the bone. The pain abated and nothing more was done until she had a massive hematemesis. She was then sent to the hospital, but the ends of the bone had penetrated the walls of the esophagus, one end working through the wall of the descending aorta as well, and the result was a massive fatal hemorrhage.

A similar fatal hemorrhage has been reported in a patient with primary tuberculous infection of the esophagus. The ulceration had extended into the descending aorta.

Bleeding from the tracheobronchial tree may be due to the presence of tuberculosis, malignant neoplasm, benign adenoma, hemangioma, broncholithiasis, or bronchiectasis. With the exception of hemangioma, the history and roentgenogram will usually establish the diagnosis. The hemangioma can usually be seen through the bronchoscope and destroyed by electrocoagulation. Bronchoscopy and biopsy are necessary to differentiate between a malignant neoplasm and a benign adenoma. Pneumonectomy should be done in those cases of carcinoma of the lung which are operable. Electrocoagulation will usually control the tendency of adenomata to bleed; removal of the calculus whenever possible will relieve broncholithiasis; lobectomy is indicated if bronchiectasis is unilateral, and postural drainage, chemotherapy and management of a possible allergy if the disease is bilateral.

In all cases presenting no definite local cause for the hemorrhage, careful general examination should be made. Cardiorenal disease with hypertension may be the main reason for the bleeding. Complete blood studies, including platelet counts and coagulation time, must be made to rule out the hemorrhagic diseases. A low platelet count is found in thrombocytopenic purpura hemorrhagica of both primary and secondary types. In the primary type splenectomy is the only procedure that has given relatively good results. The secondary type includes many of the blood dyscrasias such as pernicious anemia, mylogenous leukemia, lymphatic leukemia, aleukemic myelosis, and aplastic anemia.

Hemorrhage may occur in many of the infectious diseases. Delayed

coagulation time with a normal platelet count occurs in hemophilia, in obstructive jaundice, and in hemorrhagic disease of the newborn. In hemophilia there is a deficiency of thromboplastin; in obstructive jaundice and hemorrhagic disease of the newborn there is a deficiency of prothrombin. This can be corrected by the administration of vitamin K, but to give vitamin K in all cases of bleeding without first determining a real deficiency of prothrombin is of no value.

In all severe hemorrhages the first and most urgent concern is to control and stop the bleeding. Secondly, the depleting effects of the hemorrhage must be remedied by the use of general supportive measures. These include rest and administration of iron and, if the loss of blood has been sudden and severe, blood transfusion. Appropriate sedation may prevent a recurrence of the bleeding until the ruptured vessel has healed or thrombosed.

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OCULAR TORTICOLLIS

Report of a Case

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The term "ocular torticollis" was applied by Cuignet in 1874 to a compensatory tilting of the head in cases of paralysis of one of the muscles controlling the vertical movements of the eye. The patient unconsciously assumes this position to avoid diplopia.

The following case is presented to show the need for eye muscle studies in all cases of torticollis.

Case Report

A 57-year-old woman reported to Cleveland Clinic in October, 1944, with the complaint of "sore neck" and "spasm of neck muscles". She stated that for twelve years she had had a "drawing" of the neck, which had noticeably increased during the past two years. Examination revealed the head (chin) turned to the left, the patient having difficulty straightening her head.

There was decided apparent hypertrophy of the right sternomastoid muscle. X-ray examination of the cervical region of the spine showed a slight cervical dorsal scoliosis of the cervical and dorsal regions of the spine. Considerable osteoarthritis was present in the cervical area, and there was some calcification of the intervertebral discs.

The intervertebral spaces were narrowed below the level of the fifth cervical vertebra. The impression was osteoarthritis of spine, cervical region. Laboratory reports showed blood Wasserman and Kahn tests negative, other reports within normal limits. Blood pressure was 135/85; heart and lungs were normal.

It was believed that the patient had a spasmodic torticollis, and she was placed on physiotherapy, from which she received partial relief.

On February 27, 1946, she returned to the Clinic with symptoms in the neck as before. She had recently had her lenses changed and consequently was referred to the department of ophthalmology for determination of any contributing etiologic factors.

Ophthalmologic examination revealed visual acuity O.D. 6/9-3, O.S. 6/12. External examination negative except for ocular muscles. The fundus was negative O.U. Refraction with cycloplegia: O.D. plus 1.00 sphere combined with a plus 0.75 cylinder axis 180 in each eye, with vision corrected to 6/6. Muscle balance tests showed: at 6 meters, 6 prism diopters exophoria and 10 prism diopters right hyperphoria; at 33 centimeters, 10 prism diopters exophoria and 7 prism diopters right hyperphoria. Tests revealed a crossed and vertical diplopia. The chin was inclined to the left, with the head tilted to the right.

Operation was recommended, but the patient refused at this time. As a palliative measure she was advised to wear a clip over one eye.

Discussion

This case demonstrates ocular torticollis and its most common cause, paresis of the superior rectus muscle on the side of the head tilt, with overaction of the inferior oblique muscle on the opposite side.

Ocular torticollis must be distinguished from spasmodic torticollis, due to unilateral spastic contracture of the sternomastoid muscle, in order to avoid ineffective operative procedures.

Differential Diagnosis

Spasmodic Torticollis	Ocular Torticollis
1. Head tilt usually obvious.	1. Head tilt usually less obvious.
2. Gross contracture of sternomastoid muscle on "tilt" side of neck.	2. No true contracture of sternomastoid muscle. Slight degree of "tightness" of structures on "tilt" side of neck.
3. Head cannot be passively straightened.	3. Head can be passively straightened, but interferes with ability of patient to maintain binocular vision because of manifest vertical divergence of the visual axes. Patient "fixes" with one eye only, neglects image of other. (Suppressed). If suppression does not occur, diplopia is experienced.

4. Face always turned upward and away from side of head tilt.	4. Face usually turned slightly toward side of head tilt, and in some cases, downward.
5. Conjugate ocular movements normal.	5. Conjugate ocular movements abnormal.
6. Extra-ocular muscle balance normal.	6. Hypertropia of one eye, hypotropia of other eye. Head tilted toward hypertrophic eye.

Treatment

The treatment of ocular torticollis is primarily operative. The condition can be corrected by advancing or shortening the affected muscle. Orthoptic exercises may be necessary following operation in some cases. Prisms in low powers (never over 6^{Δ}) may be ordered if necessary. In cases of long standing it may be necessary, due to the apparent hypertrophy of the sternomastoid muscle, to do an intradural section of the anterior motor roots of the first three cervical nerves on both sides. This is usually followed by peripheral section of the spinal accessory nerve on the affected side. The correction of refractive errors has little effect on this condition.

The examination of all torticollis cases should include a complete examination of the eye muscles for possible imbalance, as ocular torticollis can be corrected by operation on these muscles. All cases of suboccipital headache and pain in the neck should be checked for vertical muscle imbalance.

Summary

1. A case of ocular torticollis has been presented.

2. A differential diagnosis between spasmodic and ocular torticollis is described.

3. The treatment of ocular torticollis is primarily operative.

4. The examination of all cases of torticollis should include the study of the eye muscles for any imbalance.

CLIMACTERIC—MALE AND FEMALE

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In women the climacteric at one time referred to seven year cycles throughout life, puberal climacteric, menopausal climacteric, and at the age of 63 the grand climacteric. Nowadays when we mention the climacteric we mean the period of a woman's life in which the function of child bearing ceases; the menopause, which is an incident in this change, is the result of hormonal readjustments and genital atrophy which result. The whole process is normal and physiological and is not a disease.

In general the menopause is considered a mark of the climacteric, although climacteric symptoms frequently precede the cessation of menstruation by months and sometimes by years, and although it is rare, typical symptoms may make their appearance as late as ten years after the menstrual flow disappears. Rarely the climacteric occurs before the age of 20, and it may occur before the menarche, as in a case which I recently reported[1] in which typical hormonal changes, headaches and hot flashes were present at the age of 16 years, before the menses appeared. On the other hand menstrual periods occasionally remain regular until the age of 65. The average age for cessation of menstrual periods is 47 years, and race or the age of onset of menstruation have not been shown to have a distinct bearing on the time of the menopause.

The Physiology of the Female Climacteric

The primary change is probably in the ovary, which gradually fails to respond to stimulation from the pituitary. Failure to ovulate regularly appears to be an early part of this change, and as a consequence the corpus luteum does not form, and progesterone is not produced. The absence of progesterone may cause abnormal bleeding but produces no other symptoms. In this anovulatory state, sufficient response on the part of the follicles may remain, to bring about in turn some alternate regeneration and regression in the endometrium, with regular cycles of uterine bleeding. Eventually follicular growth and production of follicular hormone falls to such a low level that the endometrium undergoes too little growth and regression to respond with bleeding, and the periods cease. The uterus becomes smaller. The vaginal mucosa loses its cornified epithelium, and smears from the vagina, instead of showing flat, cornified cells, show smaller, rounded cells with large nuclei from the deeper layers of the vagina together with white blood cells. There is atrophy of the cervical and vulvar glands and involution of the duct system of the

breast. The sodium, nitrogen, and water metabolism, which are affected so much by androgens, are disturbed very little by estrogens. During this time the anterior lobe of the pituitary tends to enlarge, basophile elements in it increase,[2] and excessive quantities of gonadotrophic hormone appear in the urine. The titre of urinary gonadotrophins commonly rises from a normal daily average of about 25 to 50 mouse units to 200 or even 500.

The mechanism of the symptoms so commonly associated with the menopause is not clear. Albright[3] suggested that they might be caused by the heightened levels of gonadotrophins, since these substances increase as symptoms increase and decrease with estrogen therapy. However, serious objections to this explanation can be raised. For example, high titres of gonadotrophins may be present in the urine of post menopausal women who have no symptoms. It is interesting in this connection that high titres of urinary gonadotrophins can be demonstrated in postmenopausal women who have never had any climacteric symptoms. Also, menopausal symptoms are likely to be absent in the presence of pituitary tumors in patients with high gonadotrophin excretion.

Hamblen[4] has suggested that menopausal symptoms are normally controlled by an increasing adrenal production of androgens. In regard to this theory it is interesting to consider the situation which exists in women with Addison's disease and menopause. Under these circumstances climacteric symptoms may be present and the only source of androgens in the women, namely the adrenal glands, is virtually removed. According to the theory it should follow that climacteric symptoms would be more than usually severe or more difficult than usual to control. Such has not been the case, however, in our patients who have Addison's disease and menopausal hot flashes. In them small doses of estrogens have been effective. Thus if any of the normal controlling mechanism of the menopause is present in the adrenal cortex the fact is not indicated by destruction of the gland in Addison's disease. Also, postmenopausal women with myxedema may have no climacteric symptoms in spite of the fact that urinary 17-ketosteroids are very low.

Regarding the cause of climacteric symptoms, one can only say that they are intimately connected with estrogen withdrawal in an individual previously accustomed to its presence in moderate amounts and that the exact mechanism of production of symptoms is not understood.

Clinical Manifestations

Hawkinson[5] believes that distressing symptoms occur in 75 per cent of women during the climacteric. In an analysis of 1000 cases he lists symptoms in the following frequency (table 1).

Table 1

Frequency of Climacteric Symptoms

% frequency	
95+	Nervousness Menstrual disturbances Flushes or chills
85+	Excitability Fatigability—lassitude
70+	Depression Irritability Insomnia Tachycardia, etc.
60+	Vertigo Poor memory Headaches
40+	Frigidity Numbness Occipito vertical aching

(Adapted from Hawkinson)

In 1933, the subcommittee of the Medical Women's Federation in Great Britain studied women who were not under medical care and concluded from 1197 patients that 89.7 per cent were able to carry on their usual occupations; 15.8 per cent of these had no symptoms, and only 10.3 per cent of the total were incapacitated by the climacteric.[6]

Apart from abnormal bleeding the manifestations of the climacteric which require treatment are almost entirely symptomatic. It is important, therefore, that a critical analysis be made of all the features present. Hereditary traits, tendency to emotional instability, coexisting disease, poor nutrition, factors which may cause excess nervous strain, such as overwork or domestic problems, must all be carefully evaluated. It should be borne in mind that hot flashes of mild degree may occur in women with unstable vasomotor systems who do not have ovarian failure, and moderately severe flushing may occur in the presence of arterial hypertension. Under such circumstances this symptom is likely not to be amenable to estrogen therapy.

Weight gain, which is frequently associated with the menopause, shows a tendency to special distribution of fat about the pelvic girdle

and over the trochanters. Pads of fat may often be seen anterior to the lateral malleoli. In spite of the implication that such obesity is due directly to ovarian deficiency, this has never been proved, and it appears likely that most of the weight gain is due to maintenance of a good appetite in the presence of decreasing physical activity. It can be managed properly only by diet.

Arterial Hypertension

In states in which nervous tension is heightened the blood pressure is inclined to vary excessively. Such a relationship may exist in people with unstable nervous systems and climacteric symptoms. The recent studies of Taylor[7] emphasize the fact that true arterial hypertension is not related to ovarian failure. He made a careful study of 200 women three or more years after the menopause. One hundred and seventy-nine of these patients had been surgically castrated. Hypertension existed in 13 per cent of his group, almost exactly the same incidence as shown in the general population as a whole of women between 20 and 60 years of age, according to the statistics of the Metropolitan Life Insurance Company.

Menopausal arthralgia is a term applied to mild joint pains unaccompanied by objective evidence of joint disease. When it occurs it is usually found in the small joints, shoulders, elbows, and knees at the climacteric. Such pains usually disappear promptly with estrogen therapy.

Menopausal osteoporosis may reach moderately severe proportions. It affects the spine chiefly. It is associated sometimes with pain but usually not with vertebral compression. Albright[3] recommends estrogens for this condition and reports improvement in the degree of ossification of the spine following its use. We use in addition calcium lactate, 3 grams twice daily, and 50,000 units of vitamin D per day.

Mental Depression

Mild symptoms of depression are very frequently associated with climacteric. Such symptoms are usually benefited promptly by estrogen. In my own experience I have never seen true involutional melancholia benefited materially by estrogen therapy. Improvement which may occasionally be seen is difficult to evaluate because spontaneous improvement occurs in some patients.

Diagnosis

Diagnosis of the climacteric is seldom in doubt but at times peculiar problems present themselves. Because some symptoms referable to the

climacteric occur in most women after the age of 45 it is important not to assume that concurrent disease is absent. At times fatigue and hypometabolism may raise the problem of hypothyroidism, while in others in whom excitability and tachycardia are more outspoken care should be taken to exclude hyperthyroidism.

Amenorrhea may lead to a suspicion of pregnancy. If a Friedman or Aschheim-Zondek test is used it should be borne in mind that the high excretion of gonadotrophins at the climacteric causes false positive results to occur more frequently than in earlier life. Especially in younger patients when early climacteric is suspected, more complete evaluation of the problem may be indicated. In these, vaginal smear studies and endometrial biopsies make excellent means of assay for follicular function, and when low ovarian activity is present, the degree of pituitary activity can be determined by doing an assay for gonadotrophins. We employ for this the immature mouse assay described by Albright[3] and expect over 53 and usually 105 mouse units to be excreted in twenty-four hours in cases of primary ovarian failure.

Entirely normal findings in such assays exclude ovarian deficiency. Such tests must be interpreted, however, remembering that in most instances some estrogen remains in the blood after menopausal symptoms appear.[8] Therefore, typical castrate type of smears are seldom seen, and moderately severe symptoms may exist in the presence of only slight evidence of follicular failure as judged by the smear test. In addition, smears of a deficiency type and high levels of urinary gonadotrophins continue into old age after climacteric symptoms have disappeared. However, if active estrogen therapy is given, and vaginal smears are maintained in a normal state for several weeks, any remaining symptoms can usually be rightly assumed not to result from ovarian deficiency.

In diagnosis it is essential not to overlook the possibility of malignant disease as a cause of irregular bleeding.

Treatment in Uncomplicated Cases

Symptoms may begin insidiously as increasing premenstrual tension, headache, or mastalgia. If a tendency to premenstrual edema is present, careful restriction of sodium and the use of 3 Gm. of ammonium chloride or 6 to 10 Gm. of potassium nitrate in enteric coated pills per day for ten days before the menses may be helpful. In cases in which edema is present and nervous tension is not great, small doses of benzidrine can be tried. In others mild sedation and small doses of estrogen over a similar period may give further symptomatic relief.

Many patients need no treatment.

In all uncomplicated cases confident reassurance is important, and the patient should understand the harmless nature of the condition and the lack of influence it is likely to have upon her general health and sexual life.

Attention should be given to proper rest, adequate exercise, recreation, and correct diet. Mild sedation including phenobarbital, tincture of hyoscyamus, or bromides singly or in combination is helpful.

The choice of estrogen therapy presents a problem, particularly because there are so many forms from which to choose. Stilbestrol is valuable in most cases because it is potent, orally active, and cheap. The required dose is usually about 1.0 mg. per day, but may vary from 0.25 mg. to 3.0 mg. Unfortunately it produces nausea in about 15 per cent of cases. If it does, methyl stilbestrol may be tried in approximately ten times this dose. A newer drug not likely to produce untoward symptoms is one of the hexane derivatives, which may be given in doses of 10 to 30 mg. per day. Stilbestrol dipalmitate in oil is a soap-like material which can be liquified by heat and injected intramuscularly. A single injection containing 15 or 20 mg. of stilbestrol may control climacteric symptoms for three months or more at a time. It has the disadvantage that its effects cannot be discontinued at once in the event of menorrhagia. For this reason it is admirably suited to the treatment of patients who have undergone hysterectomy. When natural estrogens are preferred or when stilbestrol disagrees, ethinyl estradiol, strongest of all estrogens, may be used. It has the advantages of potency and oral effectiveness, but may also produce nausea. Other estrogens for oral use are sodium estone sulphate (premarin), estriol glucuronide (emmenin), and estriol (theelol). They are all well borne, but weaker and more expensive than the synthetic preparations. Of the injectable natural estrogens, estradiol benzoate or propionate is the most efficient. There is a tendency to give such medicaments in inadequate doses or too infrequently, in which case the effect is unphysiologic. Estradiol benzoate in doses of 0.33 mg. (2000 rat units) three times weekly, is adequate in the majority of cases. In our hands it has shown less tendency to produce menorrhagia than has stilbestrol. Estrone (theelin) is much weaker and therefore larger doses by weight are necessary, 2.0 mg. (20,000 international units) three times weekly is sufficient in most patients and half this dose is enough in many. Few signs or symptoms of overdosage directly connected with estrogen are seen. Occasionally fullness or soreness of the breasts, a sense of fullness and discomfort in the pelvis, or an excessive vaginal discharge necessitate a lowering of the dose. Apart from these symptoms, injectable natural estrogens produce no untoward side effects, though rarely there may be seen a local allergic

type of response to the vehicle injected. There is such a variety of useful orally active estrogens available that when cost and convenience to the patient are factors to be considered the more expensive injectable estrogens are seldom indicated in the treatment of the climacteric.

A combination of small doses of androgen given with estrogen may reduce the tendency to menorrhagia, and when this tendency is not pronounced such a combination may make continued treatment possible. On the whole, androgens are much less efficient than estrogens in the control of climacteric symptoms.

Special Considerations

Pruritus vulvae is likely to be present when neurosis is a relatively large factor. If the tissues involved are atrophic, estrogens may be helpful in the treatment and may be used both as general therapy orally or by injection, and as local therapy in ointment or suppositories. Rest and sedation are important. Local alcohol injections may have to be used.

In *senile vaginitis* suppositories of estrone or stilbestrol are claimed to be helpful by increasing the activity and health of the local tissues. Local hygiene and simple measures of cleanliness are important. Local dermophytosis must be treated if present. Diabetes mellitus should be excluded by careful evaluation of urinalysis and of blood sugar levels, not only fasting but two and one-half to three hours after eating. If it is present meticulous control is indicated. In true kraurosis little good has been reported from estrogen therapy, and it may be dangerous since carcinoma sometimes appears in such cases and vulvectomy appears to be the only cure when the condition is severe.

Nymphomania may become a matter of serious concern at the climacteric. I have observed four patients with a moderate degree of this who were markedly improved on estrogen therapy. One eventually became seriously psychotic in spite of treatment.

Frigidity, especially when present to some degree previously, may be accentuated in the presence of severe ovarian failure. Estrogen therapy is of very little value in such a condition. Androgens in small doses may be helpful if the patient was normal previously but are not likely to be helpful otherwise. Ten to 20 milligrams per day of methyl testosterone orally daily may be tried. If it is used evidence of masculinization must be watched for.

Menorrhagia

Menorrhagia existing in patients at the age of 40 or beyond should be suspected as organic in origin. It is usually not due to malignant disease, though this possibility must always be kept in mind. Fluhmann[9] reports 53 patients of this type, none of whom had carcinoma. Hamblen[10]

mentions a study of 177 women between 40 and 55 years of age with polymenorrhea, menorrhagia, or metrorrhagia, 173 of whom had endometria showing only estrogen effects and 4 had adenocarcinoma. In such cases it is our practice when no evidence of local disease is found to give one course of injections of estrogen, usually estradiol-benzoate 2000 to 4000 rat units three times weekly, together with 3 or 4 injections of 10 mg. each of progesterone with each of the last few injections of estrogen, ending the course a few days before the menstrual period is expected. If the menorrhagia is not controlled, a diagnostic curettement is performed, and since endocrine therapy is not likely to produce a good result on further trial, radium is usually applied.

When uterine bleeding returns after the menopause has occurred malignancy should be considered present until it is proved not to be. Fluhmann[11] found carcinoma present in 75.6 per cent of 90 such cases, TeLinde[12] in 60 per cent of 179, and Geist and Matus[13] in 57.5 per cent of 182. Obviously a prompt diagnosis and adequate surgical measures are imperative under such conditions. In the immediate control of menorrhagia near the menopause androgens may be efficient. Testosterone propionate 25 mg. to 50 mg. per day for 4 or 5 doses may be used. Two hundred and fifty milligrams per month is less than the amount necessary to cause masculinization. Methyl testosterone 10 mg. orally daily for ten days before each menstrual period may be tried. In some cases 20 mg. per day may cause deepening of the voice and hirsutism.

Contraindications to the use of estrogens are few. These substances are, however, potentially carcinogenic, and although there is no proof that they have caused carcinoma in the human, certainly they should never be used in cases in which carcinoma is suspected, where it is known to be present, or where it has been present either in the genital tract or the breast.

Male Climacteric

The term male climacteric is a misnomer in that it implies a physiologic loss of power of production of sperm and internal secretion of the testes which, according to the term, should be expected to occur at a fairly regular time of life in all men. Such a condition has not been shown to exist. There are, however, some cases in which testicular failure appears in men past middle age and without evident cause—a functional hypogonadism. It is difficult to diagnose because there are no well established diagnostic criteria. In most instances where the diagnosis appears in the literature subjective symptoms have been depended upon.

Physiology

Attempts to explain the condition are based on the state which exists in extreme testicular failure.

After castration in adult life few anatomical changes are apparent. Beard and body hair are changed little if at all, the voice and genitalia remain grossly the same, sexual potence tends to diminish, though it may not be lost, the prostate and seminal vesicles shrink markedly. A mild degree of nervous instability and mild mental depression may occur, endurance is usually diminished, and in some cases hot flashes appear.

Urinary androgens as measured by the capon comb growth test fall, urinary 17-ketosteroids fall as a rule to about half their normal level, but not infrequently remain within normal range, and urinary gonadotrophins rise. Testosterone injections 25 mg. intramuscularly three times a week promptly remove such symptoms. In castrate men such treatment brings about a return of sexual potence, a return of ejaculate, growth of the prostate, disappearance of nervous and vasomotor symptoms and an increase in energy together with a growth of the skeletal muscles. The latter is associated with increased retention in the body of certain electrolytes, including sodium and potassium, water is retained, nitrogen is stored, and the basal metabolic rate rises.

Diagnosis

When symptoms similar to these seen after castration appear spontaneously in a man of 50 or above, and when careful examination fails to reveal the cause, testicular failure may be considered a possible explanation. Too frequently impotence is the only presenting symptom, and judging from experience, impotence is seldom due to testicular failure.

In many patients a final analysis makes it clear that the symptoms suspected of being due to male climacteric can be explained more rationally on the basis of the increasing pressure of social and business responsibilities and the concurrent increase in nervous fatigue in an aging man.

Angina pectoris has been considered an evidence of male climacteric.[14] Symptomatic improvement has been reported following the use of testosterone propionate in cases of angina pectoris and patients with peripheral occlusive vascular disease. I have seen some patients with angina pectoris who appear to obtain some symptomatic benefit from testosterone. On the whole, the results are not very impressive. Considerable symptomatic improvement may follow testosterone therapy in patients who have urinary retention, especially in those patients who have no severe mechanical obstruction. It is unlikely that testosterone ever causes any prostatic shrinkage, though it may increase the strength of the bladder and other musculature and in this way aid in bladder emptying.

In treatment of any case with testosterone one must remember that marked depression of sperm production may be brought about.

My opinion in the matter of male climacteric can be best expressed by a few facts taken from the investigation of 60 patients whom I suspected of having the condition as judged purely on the basis of history and physical examination. The chief symptoms were nervousness, emotional instability, mental depression, fatigue, decreased libido and potency, and in about one-quarter of the group, mild hot flashes.

Seven assays were done for androgens by the capon method in 6 cases. The results in brief were: in 2 of the 6, androgen excretion was subnormal; in 2, borderline; and in 2 normal.

Assays for urinary 17-ketosteroids as an index of testicular function were done 38 times in 33 cases—only 6 were within normal range and only 1 reached average normal. The mean was 5.0 mg. per twenty-four hours. The normal average lies between 7 and 14 mg. (table 2).

Table 2

Male Climacteric ?

17-ketosteroids—38 assays—33 cases		
mg./24 hr.	cases	
1—2	2	
2.1—3	1	
3.1—4	7	Improved cases assayed measured 3.1, 1.1, 4.0, 8.0.
4.1—5	9	
5.1—6	4	
6.1—7	9	
7.1—8	1	
8	1	
10.9	1	

The question mark refers to the fact that these were individuals in whom this diagnosis was originally suspected on clinical grounds alone.

Gonadotrophin assays were done on twenty-four-hour specimens of urine. Thirty-two assays by the mouse method showed 17 to be above normal, nine assays done by the rat uterine weight method showed 6 to be above normal (table 3).

These objective studies appear in the majority of the cases to bear out a pattern quite in keeping with the idea that some degree of testicular failure together with a tendency to pituitary hyperfunction exists.

In this group of 60, so far as we know at present, only 10 showed what we choose to call good clinical results from treatment with testosterone propionate. These results ranged from moderate to excellent.

Due to the symptomatic nature of the improvement its degree cannot be more accurately evaluated.

Eighty-four per cent of this group remained with little or no improvement after several weeks of therapy known to improve the symptoms which follow castration. For this reason it appears that the method of diagnosis requires improvement, and further critical evaluation of the subject is necessary before a dependable conclusion can be reached as to the position in which the term, male climacteric, should be placed in clinical medicine.

Table 3
Male Climacteric?
Gonadotrophin Assays

	Mouse Test	Rat Test	10 Improved Cases
High	17	6	6
Normal	15	3	2
Total	32	9	

10 improved cases refers to all of the cases showing distinct symptomatic improvement. Six of the improved group were known to have a high titre of urinary gonadotrophins.

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CURARE

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Curare, for which urari and woorari are synonyms, first appears in the literature in 1595 in a reference of Hakluyt to Sir Walter Raleigh's voyage up the Orinoco River to Equador. A crude extract of the drug was used by the natives of that territory on their arrows to kill enemies and animals of prey. Sir Walter Raleigh took samples of this crude drug back to England upon his return.[1]

In 1814 Watterton and Brodie suggested that the chief action of this drug was the interruption of the neuromuscular mechanism.[2] Later Claude Bernard undertook the first extensive scientific investigation of the substance, demonstrating that the site of action is at the myoneural junction and that the cause of death is anoxia from paralysis of the diaphragm.[3,4] Since 1857 curare has been used for the treatment of such conditions as tetany, tetanus, strychnine poisoning, and chorea.[5]

The drug was used by Hoffman[6] in 1879 to treat the convulsions in tetanus. The modern purified drug has been produced from samples of curare[7,8] brought from Equador to this country by Gill[9] in 1932. Curare was again employed in tetanus by Cole[10] in 1934, Mitchell[11] in 1935, and West[5] in 1936. Burman[12] treated spastic states with curare in 1939, while in 1940, 1941, and 1942, Bennett,[13] Gray,[14] and Cummins[15] used it to attenuate the convulsions of tetrazol and electric shock therapy in psychiatry.

The first use of curare in anesthesia was reported by Griffith and Johnson[16] in 1942. That year and again in 1943 Cullen[17,18] reported the use of the extract in a large series of anesthesias.

Although crystalline curarine was isolated by Preger[19] in 1864, the curare preparations were somewhat crude and variable until 1943. Three types of the drug are derived from different species of strychnos and are appropriately named for their containers: tubocurare (lengths of bamboo), calabash curare (gourds), and pot curare (clay pots).[19] They yield the alkaloids tubocurarine (and curine), curarine, and protocurarine, respectively. Of these, tubocurarine is the drug in use today and is supplied as an aqueous extract containing 20 units per cubic centimeter. The unit is the equivalent of 1 mg., as determined by the "Head-drop" crossover method.

Chemistry

The active principle of intocostrin* is d-tubocurarine. This substance

* *Intocostrin is manufactured by E. R. Squibb and Sons.*

is a curare alkaloid chemically related to strychnine but of unknown molecular formula.

The action of the alkaloid apparently is not a function of its molecular structure, as a similar action is found in unrelated drugs such as phosphonium, quaternary ammonium salts,[19,20] ethyl ether, pentothal sodium, and tribromethanol.

Mechanism of Action

The alkaloid interferes with the action of acetylcholine on striated muscle so that neither acetylcholine nor a nerve impulse can produce muscle contraction.[21]

Claude Bernard[3] showed in a classic experiment that a nerve bathed in curare can conduct an impulse which excites contraction in an uncurarized muscle.

He showed further that the muscle (frog) in which the blood vessels had been ligated responded to stimulation of the nerve supply, although the animal had previously been curarized.

Curare also has an effect on the sympathetic ganglia, blocking the transmission of nervous impulses between preganglionic and postganglionic fibers.[22] A mild effect which results in relaxation is exerted upon the smooth muscle of the intestine. These facts suggest that curare acts anywhere in the nervous or muscular system where acetylcholine is the chemical mediator.[23] There is some evidence that curare blocks the peripheral response to stimulation of the vagus.

Although the chief action of the drug is demonstrably peripheral, a central depression of respiration has been reported.[24]

Prostigmine is antagonistic to the curare action, as it inhibits choline esterase, a destroyer of acetylcholine.[21] Potassium ions have been shown to exert an anticurare action.[25]

Appearance of Effect

Relaxation follows an intravenous injection of curare in two to four minutes. The first muscles affected are those supplied by the cranial nerves, as evidenced in the un-anesthetized subject by strabismus, diplopia, nystagmus, and weakness of the eyelids, accompanied by relaxation of the muscles of mastication and those of the lower jaw and pharynx, and by impairment of the functions of swallowing and coughing. The muscles of facial expression are relaxed, and speech becomes slow and difficult. The muscles of the trunk and extremities are next involved, and this results in weakness and inability to move the body. The diaphragm is the last skeletal muscle to be affected.

An effective blood level cannot be attained by the oral administration of curare, as it is destroyed and eliminated as fast as it is absorbed.

Furthermore, some of the drug may be changed and rendered ineffective by the process of digestion, as is true of epinephrine and snake venom.

Duration of Effect

The curare effect lasts from twenty to thirty minutes, after which it seems to disappear completely, except that it can be re-established by a smaller amount of the drug than was given in the previous injection.

When properly employed a satisfactory relaxation of the skeletal muscles (excluding the diaphragm) is the usual result. Occasionally the larger dose recommended, or even a dose considered to be moderate, may cause paralysis of the diaphragm and apnea.

Tolerance

No tolerance to repeated doses of curare has been demonstrated in the course of its repeated administration to many hundreds of psychiatric patients during treatment by shock therapy.[21]

Overdose

An overdose of curare is indicated by an irregularity in the respiratory movements and apnea. There is no evidence that any organic damage results from an overdose of curare.

Fate

The alkaloid is partly destroyed by the liver and partly excreted by the kidney.[22]

Side Effects

The side effects of curare when used clinically are few and, for the most part, insignificant.

The electrocardiogram of normal and diseased hearts is not disturbed by therapeutic doses of the drug.[26] Prolonged use may cause a fall in blood pressure as a result of the muscular relaxation and attendant slowing of venous circulation.[27]

The electro-encephalogram shows a suppression of the electrical activity of the frog's brain by administration of d-tubocurarine, a property shared by di-hydrobeta erythroidine, quinine ethochloride, nicotine, and thiamine.

The relaxing effect of curare on the intestines is ordinarily of no significance in the clinical use of the drug.

Technic

Curare can be used effectively with any general anesthetic agent but is not satisfactory when used alone. This is owing in part to the discomfort experienced by a patient so-treated, who is unable to control the vocal cords and the muscles of the throat and jaw which help to maintain an adequate airway.

When used with cyclopropane, an initial dose of 60 units is injected intravenously at the time that the skin incision is made. If this fails to provide sufficient relaxation, one-half to two-thirds of this dose is added in three to five minutes.[22] A similar supplemental injection is made as the effect begins to disappear or when more relaxation is needed. The initial injection varies with different anesthetists but ranges from 60 to 200 units.[1,17,21] The larger initial doses result in apnea for periods up to a half-hour and demand the continued use of artificial respiration, preferably with an intratracheal tube in place. The technic is essentially the same for use with pentothal or nitrous oxide, but when combined with ether the dose must be diminished by two-thirds, owing to the curare-like action of ether itself.

Curare has been used in both extremes of life, for many different types of operations, and in the presence of many complications.

Contraindications

Three contraindications to the use of curare have been cited. Myasthenia gravis, on account of the close resemblance of its symptoms to the curare effect, forbids administration of the drug. Its use is inadvisable when the anesthetist is unable to perform artificial respiration on account of such factors as the position of the patient and respiratory obstruction. Impaired renal function which may retard the elimination of the drug has been cited as a contraindication,[19,21] but other anesthetists do not consider this a serious objection.

Complications—Postanesthetic

There has been no reported organic damage which results from the use of curare. Untreated apnea, however, may lead to hypoxea.

At Cleveland Clinic curare is used as a supplement to the general anesthesia induced by ether, tribromethanol, nitrous oxide with oxygen, and pentothal. It is most frequently employed to improve exposure and facilitate closure during abdominal operations, thus supplementing a spinal anesthetic combined with pentothal.

It is serving to supplement an increasing number of pentothal anesthesias given for laryngoscopy, laryngeal intubation, bronchoscopy,

and esophagoscopy. In this type of procedure the curare (usually 60 units) is given as soon as the venipuncture is made, the needle then being flushed by the withdrawal and reinjection of 1 or 2 cc. of blood before attaching the pentothal syringe or tubing. This precaution is taken in order to avoid injecting the precipitate which results from mixing pentothal and the curare extract in the concentrations generally employed. The pentothal anesthesia is then begun immediately, the patient going to sleep before the discomfort of the curare effect appears.

The relaxation afforded by the curare greatly improves the exposure of the larynx (previously cocainized) for biopsy or intubation and is of especial value in short, thick-necked, heavy smokers who have a hyperactive pharyngeal reflex.

In some patients spinal or caudal anesthesia is contraindicated because of an inflamed condition of the skin in the area of the injection. When these patients require treatment for anorectal diseases, pentothal and curare provide satisfactory relaxation.

Conclusions

Curare extract (intocostrin) contains an alkaloid of unknown molecular formula which blocks the neuromuscular passage of impulses. This effect is much more pronounced in skeletal muscle, and it is this quality which renders the agent useful to the anesthetist. The only significant danger from its use is paralysis of the diaphragm, which results from the use of larger doses. The resulting apnea can be readily controlled by artificial respiration.

The development of curare represents a significant advance in anesthesiology.

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ACUTE LEFT VENTRICULAR FAILURE

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Acute left ventricular failure, characterized by an agonizing struggle for air, is terrifying to the patient, family, and physician. The seizure is distinctive, therefore most contemporary descriptions are similar. Probably the first account of this syndrome was that of Aretaeus of Cappadocia.[1] His words paint a picture that has been little improved upon in the 2000 years since his death. In patients with paroxysmal nocturnal dyspnea, "the cheeks are ruddy; eyes protuberant, as if from strangulation; . . . voice liquid and without resonance; a desire of much and of cold air; they breathe standing, as if desiring to draw in all the air which they possibly can inhale; and, in their want of air, they also open the mouth as if thus to enjoy the more of it; pale in the countenance, except for the cheeks, which are ruddy; sweat about the forhead and clavicles; cough incessant and laborious; expectoration small, thin, and cold, resembling the efflorescence of foam; neck swells with the inflation

of the breath; the praecordia retracted; pulse small, dense, compressed; and if these symptoms increase, they sometimes produce suffocation, after the form of epilepsy."

Following in the footsteps of Aretaeus, many students of heart disease (White,[2] Weiss,[3] Ernstene,[4] Blumgardt,[5] Smith,[6] Robb,[3] Wolferth,[7] Harrison,[8] Prinzmetal,[9] Christie,[10] Hope[11]) have written of the mechanism and treatment of this syndrome in recent years.

The large number of reports belies the relative infrequency of this state, but, on the other hand, emphasizes its impressive nature. With the exception of 250 patients reported by Palmer and White,[2] 82 by Weiss and Robb,[3] and 40 by Ernstene and Knowlton,[4] most other reports include few patients.

The term "acute left ventricular failure" indicates that the left ventricle is subjected to disproportionate strain because of hypertensive vascular disease, coronary artery disease, or valvular defect. Thus, in Weiss and Robb's[3] report of 82 cases, 53 per cent had hypertension, 20 coronary sclerosis, 20 syphilitic aortitis, 6 rheumatic heart disease. Ernstene and Knowlton[4] observed a similar distribution.

Few manifestations of underlying cardiac disease more certainly herald early death, particularly when the attacks occur more often than once a day and are associated with gallop rhythm or pulsus alternans.[2] The serious import of the syndrome is indicated by the average duration of life after the first attack. Palmer and White[2] found that of 250 patients, 59 were dead within the first six months, and an additional 69 within the first two years.

It seems worthwhile to re-examine the published evidence and add to it our experience gathered in the past years at the Indianapolis City Hospital and more recently at Cleveland Clinic.

Analysis of Patient Records

Twenty patients with acute left ventricular failure were observed (table). Seven of the 20 had essential and 13 malignant hypertension. One patient had six attacks and finally died of a cerebral hemorrhage. Most of them had only one or two attacks, and one was immediately fatal.

Four patients while ambulatory were observed to have paroxysmal auricular tachycardia at some time during the course of the disease. The records of 10 others showed the occurrence of extrasystoles frequently enough to have impressed the patient or the examiner. No irregularities were recorded in the remaining 6.

The average duration of life after the first attack was 1.3 years. Only 2 patients are still alive—1 with malignant hypertension has lived thirty-

six months and 1 with essential hypertension has lived eighteen months following such symptoms.

Treatment

The table indicates the type of treatment used to control the attacks. The usual management follows:

1. The nurse or relatives are instructed to assist the patient to a sitting or, if possible, standing position.

2. Sixteen milligrams of morphine sulfate is administered subcutaneously or, if possible, intravenously.

3. If bronchospasm is particularly severe, 0.5 Gm. of aminophylline in 10 cc. of saline solution given intravenously will often produce striking relief. This drug can be combined in the same syringe with the morphine.

4. If the patient is still in distress, the venous return to the heart should be reduced by withdrawal of 600 to 800 cc. of blood. However, the inconvenience of this procedure and the liklihood of coexisting anemia make bloodless phlebotomy more practical. This procedure, first advocated by Chrysippus of Cnidos about 380 B.C., is the application of tourniquets to all four limbs. If blood pressure cuffs are used, inflation to a point just greater than diastolic pressure is usually effective; if these are not available, constriction adequate to occlude venous circulation is necessary. This will pool as much as 1700 cc. of blood in the venous bed of the extremities. Treatment should be continued until symptoms are relieved. Caution should be exercised in removing the tourniquets lest the sudden return of large volumes of blood to the circulation cause more ventricular strain.

5. If the patient has not yet been digitalized this should be done as soon as the acute attack is controlled. The oral route of administration is satisfactory.

6. The patient should be kept on a maintenance dosage of digitalis following an attack. Moderate restriction of sodium from the diet accompanied by adequate amounts of water by mouth and the occasional use of mercurial diuretics are helpful in preventing further attacks.

Discussion

The mechanism of acute left ventricular failure must account for the characteristics implied in the term "paroxysmal nocturnal dyspnea", which is often used to describe it. The abrupt onset is probably its most distinguishing characteristic, yet the most difficult to explain. Unpleasant dreams, poorly tolerated position during sleep,[14] prolonged coughing,[15] deep breathing, sudden skeletal movement, increased blood volume,[16] pulmonary engorgement,[17] and early congestive heart failure[3]

have all been suggested as precipitating agents. However, the stereotyped nature of this phenomenon and the frequent absence of one or many of these stimuli offer meager support for any one of them as the sole excitant.

The nocturnal occurrence of attacks is less difficult to understand. Weiss and Robb[3] were able to find evidence of pulmonary engorgement and early fluid retention in all of their patients with this syndrome. That the recumbent position places the pulmonary circulation at a further disadvantage is evident from the observations of Hamilton and Morgan,[18] who showed that the lungs then serve as a reservoir for the blood of the extremities.

Not only is the lung capacity less while the patient is in the recumbent position (Hurtado and Fray[19]), but the vital capacity is decreased by 26.7 per cent, as demonstrated by Christie and Beams[10] in their study of the effect of position on the vital capacity of patients with heart disease.

Any or all of these factors could effect the abnormal physiologic processes responsible for the signs and symptoms of acute left ventricular failure, provided a trigger-mechanism capable of creating a sudden decrease in left ventricular output and resulting increase in pulmonary engorgement were present. That this actually can be true was demonstrated by Ernstene and Lawrence,[20] who observed a typical attack in a person with a large thrombus occluding the mitral valve. The explosive nature of the attack strongly suggests that most of them might have their inception within the wall of the abnormal left ventricle. It is well known that showers of ventricular extrasystoles and paroxysmal auricular tachycardia are not unusual among patients with left ventricular disease. These recurrent arrhythmias can temporarily decrease left ventricular output. With the conditions that have been shown to exist in the pulmonary circuit when a person with heart disease sleeps, any slight change in the output of the left ventricle could well upset the precarious relationship between right and left ventricular output so that pulmonary edema ensues.

As with other suggestions, this concept must remain theoretical until electrocardiographic evidence of such arrhythmias immediately preceding acute attacks can be obtained. However, it is noteworthy (table) that of the 20 patients observed, 4 had recurrent paroxysmal auricular tachycardia while ambulatory and 10 had frequent showers of extrasystoles. These observations were made in retrospect, and the others could have had irregularities not significant enough to record prior to the attack. It is also of interest that the adequate use of digitalis after acute left ventricular failure is helpful in preventing future attacks, as well as in controlling cardiac irregularities.

Summary

1. There is abundant evidence that pulmonary engorgement accompanies the recumbent position and sleep in patients with left ventricular heart disease.

2. Because 14 of the 20 patients reported here had paroxysmal cardiac irregularities while ambulatory, the suggestion is offered that if this occured during sleep, left ventricular output might be sufficiently decreased to precipitate attacks of paroxysmal nocturnal dyspnea.

3. The treatment found most useful in our hands includes:

(a) immediate assumption of sitting or upright position,
(b) intravenous morphine and aminophylline,
(c) bloodless phlebotomy,
(d) digitalization and the use of diuretics as prophylaxis against future episodes.

Table

Summary of Treatment and Course of 20 Hypertensive Subjects Who Had Acute Left Ventricular Failure

Age	Diagnosis	No. of Attacks	Treatment	Duration of life after first attack		Cardiac Irregularity
				living	dead	
56	Essential Hypertension	3	Sitting position Morphine Tourniquets		12 mo.	Extrasystole
36	Essential Hypertension	2	Sitting position Morphine Tourniquets		20 mo.	Extrasystole
42	Malignant Hypertension	3	Standing position Morphine		3 mo.	Paroxysmal auricular tachycardia
48	Malignant Hypertension	2	Standing position Morphine		15 mo.	Paroxysmal auricular tachycardia
44	Malignant Hypertension	1	Standing position Morphine		16 mo.	Extrasystole
29	Essential Hypertension	2	Sitting position Morphine		20 mo.	Extrasystole
7	Malignant Hypertension	1	Sitting position Morphine Tourniquets		4 mo.	Paroxysmal auricular tachycardia

Summary of Treatment and Course of 20 Hypertensive Subjects Who Had Acute Left Ventricular Failure—Continued

Age	Diagnosis	No. of Attacks	Treatment	Duration of life after first attack		Cardiac Irregularity
				living	dead	
54	Malignant Hypertension	6	Sitting position Morphine Tourniquets		17 mo.	Extrasystole
49	Malignant Hypertension	2	Standing position Morphine	36 mo.		Paroxysmal auricular tachycardia
46	Malignant Hypertension	1	Standing position Morphine		8 mo.	Extrasystole
38	Malignant Hypertension	1	Standing position Morphine		13 mo.	
42	Essential Hypertension	2	Sitting position Morphine Phlebotomy		12 mo.	
45	Malignant Hypertension	1	Sitting position Morphine Tourniquets		16 mo.	
51	Malignant Hypertension	1	Sitting position Morphine Tourniquets		1 mo.	
53	Malignant Hypertension	1	Sitting position Morphine Tourniquets		1 mo.	Extrasystole
35	Malignant Hypertension	2	Standing position Morphine		2 mo.	Extrasystole
39	Essential Hypertension	3	Sitting position Morphine Tourniquets		24 mo.	Extrasystole
22	Essential Hypertension	2	Standing position Morphine		16 mo.	Extrasystole
45	Essential Hypertension	1	Standing position Morphine	18 mo.		
46	Essential Hypertension	2	Sitting position Morphine Tourniquets		20 mo.	

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